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# CREATIVITY AND PSYCHOPATHOLOGY

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*We have many books and articles on great men, their genius, their heredity, their insanity, their precocity, their versatility and the like, but, whether these are collections of anecdotes such as Professor Lombroso's or scientific investigations such as Dr. Galton's, they are lacking in exact and quantitative deductions. Admitting that genius is hereditary, or, what is more doubtful, that it is likely to be associated with insanity, we have only the 'yes' or 'no' as our answer. But this is only the beginning of science. Science asks how much? We can only answer when we have an objective series of observations, sufficient to eliminate chance errors.*

A Statistical Study of Eminent Men  
J. MCKEEN CATTELL, 1903

## ABSTRACT

The *Mad Genius* is a recurring stereotype of contemporary cultural expression. However, starting with Lombroso's investigation of genius and madness in 1888, recent decades have seen an increasing number of empirical studies suggesting that there really is an association between creativity and psychopathology. Still, taken together, the empirical support is unconvincing - largely due to a heavy reliance on biographical data and small cohorts. The primary aim of this thesis is therefore to investigate the question of a possible association between creativity and psychopathology using large scale population based epidemiological methods.

The proposed association of creativity and psychopathology has often been placed in an evolutionary context, where the burden of psychopathology is compensated for by the advantage of increased creativity. The secondary aim of this thesis is to elucidate if a putative association between creativity and psychopathology may be mediated through genetic factors under positive selection.

In our first study (study I), based on Swedish national registries, the likelihood of holding a creative profession (artistic and scientific occupations) in individuals ( $n \sim 300\ 000$ ) with schizophrenia, bipolar disorder or unipolar depression and their healthy relatives was compared to that of controls. Results demonstrated that individuals with bipolar disorder and healthy siblings of people with schizophrenia or bipolar disorder are overrepresented in creative professions. We followed up these findings in study II using a dataset with a considerably larger sample of patients ( $n \sim 1\ 200\ 000$ ) to survey other psychiatric diagnoses and to validate previous findings.

Study IV investigated the notion that bipolar disorder is common in prominent historical leaders, e.g., Winston Churchill, Abraham Lincoln, and Napoleon Bonaparte. Results showed that individuals with bipolar disorder without comorbidity and their healthy siblings were overrepresented in the highest strata of officer suitability, a rating of leadership potential. The siblings were also overrepresented in executive professions, specifically in the subgroup of political professions.

In study III we addressed the evolutionary framework by investigating the fertility of individuals with psychiatric disorders and their healthy siblings. A total of  $\sim 2.3$  million individuals were included. With the exception of women with depression, patients had significantly fewer children than the general population.

The evolutionary hypothesis was further investigated in study V, where we systematically reviewed the genetics of creativity and estimated the heritability of creativity in two new original studies.

## ABSTRACT

Results support a genetic component in creativity, and for the first time suggest that this is contingent on sex.

In conclusion, this thesis provides support for a familial cosegregation of both schizophrenia and bipolar disorder with creativity, and suggests that this may be mediated through a genetic mechanism. Results do not support, however, that any psychiatric disorder *per se* is under positive selection.

LIST OF PUBLICATIONS

- I. SIMON KYAGA, Paul Lichtenstein, Marcus Boman, Christina Hultman, Niklas Långström, Mikael Landén. *Creativity and Mental Disorder: Family Study of 300 000 People With Severe Mental Disorder*. Br J Psychiatry, 2011, 199, 373-9
- II. SIMON KYAGA, Mikael Landén, Marcus Boman, Christina M Hultman, Niklas Långström, Paul Lichtenstein. *Mental Illness, Suicide and Creativity: 40-year Prospective Total Population Study*. J Psychiatr Res, 2013, 47, 83-90
- III. Robert A. Power, SIMON KYAGA, Rudolf Uher, James H. MacCabe, Niklas Långström, Mikael Landén, Peter McGuffin, Cathryn M. Lewis, Paul Lichtenstein, Anna C. Svensson. *Fecundity of Patients With Schizophrenia, Autism, Bipolar Disorder, Depression, Anorexia Nervosa, or Substance Abuse vs Their Unaffected Siblings*. JAMA Psychiatry, 2013, 70, 22-30
- IV. SIMON KYAGA, Paul Lichtenstein, Marcus Boman, Mikael Landén. *Bipolar Disorder and Leadership – A Total Population Study*. Submitted
- V. SIMON KYAGA, Alexander Ploner, Fredrik Ullén, Paul Lichtenstein, Patrik Magnusson, Mikael Landén. *Heritability of Creativity – Systematic Review and National Study*. Manuscript

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## LIST OF ABBREVIATIONS

BWAS	Barron-Welsh Art Scale
CAQ	Creative Achievement Questionnaire
CDR	Cause of Death Register
CI	Confidence Interval
DSM	Diagnostic And Statistical Manual of Mental Disorders
DZ	Dizygotic
FR	Fertility Ratio
ICD	International Statistical Classification of Diseases and related Health Problems
IQ	Intelligence Quotient
LISA	Longitudinal Integration Database For Health Insurance and Labor Market Studies
MGR	Multi-Generation Register
MZ	Monozygotic
NPR	National Patient Register
OR	Odds Ratio
QED	Quasi-Experimental Design
SALTY	Screening Across The Life-Span Twin Younger Cohort Study
SD	Standard Deviation
SSYK	Swedish Standard Classification of Occupations
STR	Swedish Twin Registry
TEMPS-A	Temperament Evaluation of Memphis, Pisa, Paris, and San Diego

# 1 Introduction

THE ESSENTIAL QUESTION investigated by this thesis was already placed by Aristotle two millennia ago: ‘Why is it that all those who have become eminent in philosophy or politics or poetry or the arts are clearly melancholics and some of them to such an extent as to be affected by diseases caused by black bile?’ (Aristotle & Barnes, 1984).

Today, the genius-madness link remains one of the most debated in contemporary research on creativity (James C. Kaufman & Sternberg, 2010). Authors have taken completely contradictory positions; some arguing that psychopathology have nothing to do with creativity while other claim the two to be deeply entwined. Many times these arguments are passionate and often little founded in empirical research.

This thesis aims to present original research conducted with large scale epidemiological methods related to the question of creativity and psychopathology. The main question of a putative association between creativity and psychopathology is considered in study I and II, whereas study III – V investigates questions related to this idea.

## 1.1 CONTEMPORARY RESEARCH ON CREATIVITY

While there had been early attempts to characterize the creative process, it was J. P. Guilford who introduced creativity as an important field for psychological research. In his 1950 inaugural address to the American Psychological Association (Guilford, 1950), Guilford characterized creativity as the most important resource available to human society. He said that efforts to promote creativity would pay high dividends for society as a whole. Guilford also promoted the use of *psychometrics*, the objective measurement of creativity, and argued that *divergent thinking* is at the heart of the creative process. Divergent thinking does not result in one right answer, but rather in a number of possible solutions to an open ended problem (James C. Kaufman & Sternberg, 2010).

Other researchers have emphasized other aspects of creativity. For example, a fundamental difference has been made between genius and everyday creativity, also referred to as *big-C* and *little-c*, respectively (James C. Kaufman & Sternberg, 2010). From a research perspective these two aspects are often investigated with completely different methods. Research in big-C is often centered on creative *products*, whereas research in little-c more often is directed at the subjective experience of the creative *process*.

The creative *process* and *product* are together with *personality* and *press*, frequently referred to as the four p:s of creativity research (James C. Kaufman & Sternberg, 2010). Research on *personality* investigates traits that are indicative or contraindicative for creative behaviors. For instance creative artists and scientists share traits such as higher openness to new experiences, ambition, and reduced conventionality and

conscientiousness, compared to both less creative colleagues and the population in general (Feist, 1998). One of the most popular hypotheses on the *creative process* is by Wallas from 1926 dividing the creative process into the four stages: *preparation, incubation, illumination, and verification* (1926). Finally, creativity depends on the setting, which is investigated in studies of *press* (from pressures). For instance, creativity tends to flourish in an environment providing both resources and tolerance (Florida, 2002).

## 1.2 LITERATURE REVIEW OF CREATIVITY AND PSYCHOPATHOLOGY

This section reviews the current state of knowledge on the association between creativity and psychopathology. A total of 98 original studies, make up the core of this review. The major part of studies reviewed concerns psychotic disorders, such as schizophrenia or bipolar disorder, or subsyndromal psychotic features, e.g., schizotypy. In line with investigations on subsyndromal symptoms, some studies also investigate non-diagnosed relatives of patients. These studies are also important since a genetic mechanism underlying the association of creativity with mental disorder has been proposed.

### 1.2.1 Background

The first comment made on the association of genius and madness is often attributed to Aristotle (Akiskal & Akiskal, 2007). Later, similar observations were made by Seneca the younger, Dryden, and others (Motto & Clark, 1992). While comments like those made by Aristotle have been frequent in Western history, some argue that it was not until the 19<sup>th</sup> century that the concept of the mad genius really emerged (Becker, 2000). In 1888, the Italian psychiatrist Cesare Lombroso argued that genius was a constitutional defect (1891). Increasingly, however, Lombroso was questioned and many authors following Lombroso adopted a less extreme view.

### 1.2.2 Search strategy

The search strategy for the present review is based on the following criteria: all articles, letters, meeting abstracts or book chapters published in English attained through the MESH-terms (*creativity*) AND (*mental disorder*) in MEDLINE and Web of Science. The search yielded a total number of 690 and 140 hits, respectively, which after examining the titles and abstracts were pruned to include exclusively original studies. This resulted in a total of 98 original studies published until December 2013. One study was published in 1959, whereas all other studies were published after 1970. The included articles are presented according to five broad categories; a) studies investigating psychotic

and mood disorders (Table 1), b) studies primarily investigating neurodevelopmental disorders (Table 2), c) studies primarily investigating substance use/abuse disorders (Table 3), d) studies primarily investigating neurological disorders (Table 4), and e) studies investigating other mental disorders (Table 5).

### 1.2.3 Psychotic and mood disorders

The major part of studies reviewed concerns psychotic disorders, such as schizophrenia and bipolar disorder. One of the reasons for this is undoubtedly that schizophrenia and bipolar disorder represent the prototypical severe psychiatric illnesses, which have defined psychiatry since Kraepelin's days (Shorter, 1997). In fact, the debate has been intense on whether it is schizophrenia or bipolar disorder that is associated with increased creativity. This discussion was clearly articulated in the *Journal of Creativity Research*, when Louis A. Sass criticized the conclusions by Kay Redfield Jamison and others, who drew a link between bipolar disorder and creativity (L. A. Sass, 2000). He criticized Jamison for an overly romantic view of creativity, not corresponding to how creativity is manifested in a modernist and post-modern world. Jamison responded that she in no way questioned that creativity to some extent is time and culture bound, or the possibility of a connection between schizophrenia and creativity (K. R. Jamison, 2000). However, she suggested that at the time empirical support for an association between bipolar disorder and creativity was present, rather than for schizophrenia and creativity. Since then, additional studies have been conducted, and they have in several cases provided support for an association between bipolar disorder and creativity, without correspondingly providing similar support for a link between schizophrenia disorder and creativity. However, several studies have pointed to a connection between subsyndromal psychotic symptoms (e.g., schizotypy) and creativity. Schizotypal traits can be broadly grouped in three categories: positive schizotypy (unusual cognitive and perceptual experiences, tendency to magical ideation, reference, and paranoid thoughts), negative schizotypy (social isolation and reduced emotional expression), and cognitive disorganization (poor attention and concentration as well as poor decision-making) (Claridge et al., 1996; Mason & Claridge, 2006). The associations reported for creativity are consistent with positive schizotypy. In line with investigations on subsyndromal symptoms, some studies have also investigated non-diagnosed relatives of patients with either schizophrenia or bipolar disorder, demonstrating increased creative abilities in these individuals. The assumption is here that relatives of patients share traits but demonstrate lower symptom severity, which might be more beneficial for creativity than the fulminant disorder (Richards, Kinney, Lunde, Benet, & Merzel, 1988).

### 1.2.3.1 *Schizophrenia*

#### 1.2.3.1.1 Patients with schizophrenia

Many of the earliest studies reviewed examine schizophrenia in relation to creativity. On the whole, studies have failed to demonstrate increased creative abilities in patients with schizophrenia. For example, Herbert already in 1959 described a group of 60 patients, including those with schizophrenia, admitted from 1928 to 1955 (1959). There was no increased rate of artistic occupations in the group. Andreasen et al. examined both patients with schizophrenia and bipolar disorder (1974), finding that patients with schizophrenia tended to be over-inclusive and showing less richness and bizarreness in writing, compared to the writers and those with a history of mania in the same study. Similar results were reached by Dykes et al. who judged that schizophrenic patients' widening of attention was involuntary leading to a deleterious effect on creative performance (1976). Patients with schizophrenia also performed worse on the Remote Associate Test in a study by Folley et al. (2005), and other creative tests in a study by Abraham et al. (2007). Abraham et al. concluded that there was no obvious negative correlation between executive functions and creative abilities. Jaracz et al. affirmed the latter demonstrating that lower scores on the inventiveness part of the Berlin Intelligence Structure Test positively correlated with lower scores on Wisconsin Card Sorting Test (2012). Studies investigating prominent personalities have rarely found a greater proportion of schizophrenia among them. Andreasen, for example, examined 30 creative writers and found many of them suffered from affective disorders, but none afflicted with schizophrenia (1987).

#### 1.2.3.1.2 Psychoticism and schizotypy

While few studies have shown a link between schizophrenia disorder and creative abilities, many studies have established a link between subsyndromal psychotic symptoms, i.e., psychoticism or schizotypy, with creativity. Kidner demonstrated such a relationship between Eysenck's Psychoticism scale and the originality and fluency scores from a creative index (1976). Kline found a similar relationship between Eysenck's Psychoticism scale and verbal fluency, but in males only (1986). Schulberg et al. showed a correlation between positive schizotypy and creativity as measured by the Barron-Welsh Art Scale (BWAS) and How Do You Think (1988). Corresponding findings were made by Kinney et al. using the Lifetime Creativity Scales (2000), and Weinstein et al. using the Remote Associate Test and a written fluency test (2002). Folley et al. observed enhanced divergent thinking abilities in schizotypal subjects compared to both healthy controls and patients with schizophrenia (2005). By using near-infrared optical



spectroscopy, these authors suggested that the increased ability in divergent thinking was associated with activation of the right prefrontal cortex. Similar suggestions had been done in the study by Weinstein et al. referenced above (2002). In a larger study of 425 British adults (269 females, 156 males), positive schizotypy, assessed by *unusual experiences* in the O-LIFE inventory, was associated with increased mating success mediated through accomplishment in creative activities (Nettle & Clegg, 2006). The same author also demonstrated that while poets and artists were similar to schizophrenic patients with regards to unusual experiences, they exhibited less *introverted anhedonia*, i.e., negative schizotypy, compared to patients with schizophrenia (Nettle, 2006). Similar findings of O-LIFE and creativity were made by Burch et al. (2006), although Claridge et al. was unable to replicate the correlation between positive schizotypy and divergent thinking (2009). Nelson et al. was able to show an association between a phenomenological approach to creativity and O-LIFE (2008). Finally, Miller et al. using another inventory for schizotypy (Schizotypal Personality Questionnaire) in 225 university students again concluded that there were significant correlations between positive schizotypy and verbal and drawing creativity (2007). However, the increase in creative abilities was mainly due to a correlation between positive schizotypy and Big Five personality trait of *openness to experience*.

#### 1.2.3.1.3 Relatives to patients with schizophrenia

In line with studies of subsyndromal psychotic symptoms rather than fulminant schizophrenia, some authors have investigated non-diagnosed relatives of patients with schizophrenia. Among the first was Karlsson, who based on three large books on genealogy published by different authors and covering all regions of Iceland, concluded that relatives (n=486) of patients with schizophrenia were more often represented in *Who's Who* compared to the general population (1970). Since certain branches were high in both psychosis and listings in *Who's Who*, the author concluded that a genetic explanation for the overall findings was likely. The genetic basis, was also advanced by Keri, who in a study of 200 healthy individuals demonstrated that the Neuregulin 1 gene (SNP8NRG243177/rs6994992) was associated with scores on the Creative Achievement Questionnaire (CAQ) and the Just Suppose subtest of the Torrance Test of Creative Thinking (2009). The highest creative achievements and creative thinking scores were found in people who carried the T/T genotype, which previously has been shown related to increased psychosis risk. Karlsson followed up his own results in a study of 8 007 relatives of psychotic persons, and concluded that these were overrepresented as authors of published books (1984). A much smaller study by Kauffmann based on the six most

socially and intellectually competent children of mothers with schizophrenia and other psychiatric disorders, concluded that these children were more creative compared to controls (1979).

### 1.2.3.2 *Bipolar disorder*

#### 1.2.3.2.1 Patients with bipolar disorder

While few studies have affirmed an association between schizophrenia disorder and creative abilities, the opposite is true for mood disorders and especially bipolar disorder. One of the most well known studies was initiated by Andreasen investigating 30 creative writers included in the Iowa Writers' Workshop, and their first-degree relatives (1987). The workshop is one of the oldest and most widely recognized creative writing programs in the United States. Eighty percent of the writers, compared to 30 percent of controls, had been suffering an affective disorder sometime in their lives. A remarkably high proportion of the writers suffered from bipolar disorder (writers: 43 percent vs. controls: 10 percent). Jamison similarly investigated 47 British writers and artists, demonstrating that 38 percent had been treated for an affective illness (1989). The playwrights had the highest overall rate (63 percent) of an affective illness, but only poets (16.7 percent) had been treated with more serious interventions, such as hospitalization, lithium, ECT, etc. for bipolar illness. Ludwig similarly established an increased rate of manic episodes in a cohort based on biographies published in the New York Times Book Review from 1960 to 1990 (1992, 1995). This increase was further pronounced when only those active within classical creative occupations were included (~3 percent vs. ~10 percent). Post examined 291 World famous men in science, thought, politics, and art, demonstrating an increase in depressive conditions, with psychoses entirely restricted to affective varieties (1994). Again, writers were singled out with a total of 72 percent having experienced a mood episode. Post then followed up his study with another study of ~100 well-known diseased British and American prose and play writers (1996). Results indicated psychopathology within the affective spectrum in 80.0 percent of poets, 80.5 percent of novelists / poets, and in 87.5 percent of playwrights. Richards et al. investigated patients with bipolar disorder, cyclothymes, and relatives of patients using the Lifetime Creativity Scales (1988). Results failed to show an increase of creativity in only patients vs. controls, but an increase in the combined group of patients and relatives vs. controls. Simeonova et al. explored 40 adults with bipolar disorder, 20 bipolar offspring with bipolar disorder, 20 bipolar offspring with ADHD, and 18 healthy control parents and their 18 healthy control children using the BWAS (2005). Patients were diagnosed by means of the Structured Clinical Interview for

## INTRODUCTION

DSM-IV Axis I Disorders. Results revealed that adults with bipolar disorder compared to controls scored (120 percent) higher on the BWAS Dislike subscale. Mean BWAS Dislike subscale scores were also higher in offspring with bipolar disorder (107 percent higher) and offspring with ADHD (91 percent higher) than in healthy control children. The results were followed by a study by Santosa et al., where patients with bipolar disorder (but not those with major depressive disorder) and creative controls scored significantly higher on total BWAS compared to normal controls (2007).

A specific question related to creativity and bipolar disorder has been the impact of lithium treatment. Three studies investigate this specifically, although only two provide clear results. Shaw et al. determined the effect of lithium on the productivity and idiosyncrasy of written associations in 22 euthymic outpatients with affective disorder (1986). Lithium discontinuation produced a significant increase in associational productivity and idiosyncrasy, while restoration of lithium dosage reversed both these effects. On the other hand, Schou interviewed 24 'manic depressive' artists with lithium treatment about their creative abilities during treatment, and most (n=12) reported beneficial effects on artistic productivity in the long run (1979).

### 1.2.3.2.2

#### The affective temperament

Some studies have investigated the affective temperament in relation to creative behavior. For example, Strong et al. showed that *cyclothymia* and *dysthymia* assessed by the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A) was related to BWAS Total scores and BWAS Dislike subscale scores (2007). Srivastava et al. have demonstrated that BP, major depressive disorder, and creative controls, compared to normal controls, display increased TEMPS-A Cyclothymia scores (2010). Similarly, Vellante et al. demonstrated that creative people scored higher on the cyclothymic, hyperthymic and irritable subscales of the TEMPS-A, while scores on the CAQ was positively associated with cyclothymic and hyperthymic, and partly with irritable subscales of the TEMPS-A (2011).

### 1.2.3.2.3

#### Relatives to patients with bipolar disorder

Studies of relatives to patients with bipolar disorder have also revealed interesting results. About a quarter (n=124) of the index patients in Karlsson's study on 487 relatives of patients with psychosis were 'manic depressives' (1970). In Richards and co-workers' study investigating patients with bipolar disorder, cyclothymia, and relatives to patients using the Lifetime Creativity Scales, results suggested higher creativity among normal index relatives than among 'manic

depressives' ( $p < .10$ ) (1988). As mentioned previously, in the study by Simeonova et al. mean BWAS Dislike subscale scores were higher in bipolar disorder offspring with bipolar disorder (107 percent higher) and bipolar disorder offspring with ADHD (91 percent higher) than in healthy control children (2005).

TABLE I. SUMMARY OF STUDIES INVESTIGATING PSYCHOTIC AND AFFECTIVE DISORDERS

REFERENCE	STUDY SAMPLE	ASSESSMENT OF MENTAL DISORDER	DEFINITION OF CREATIVITY	FINDINGS
(Herbert, 1959)	60 patients admitted to The New York Hospital Westchester Division 1928 to 1955.	Personality disorders, addiction, psychoneuroses, schizophrenia, paranoid, manic-depressive, melancholia, organic mental reactions.	Artistic occupation.	» Increase in personality disorders—diagnosed as 'psychopathic personality'.
(Karlsson, 1970)	486 relatives of psychotic persons born 1881-1910, identified from the records of the Kleppur Mental Hospital in Reykjavik, Iceland. Relatives were born 1851-1940. Three kindreds and their branches were specifically investigated.	Schizophrenia: n=362, manic depressive: n=124.	Listed in the Who's Who.	» First-degree and second-degree relatives of patients more often listed in Who's Who compared to the general population. » Same branches are high in both psychosis and listings in Who's Who.
(N. J. C. Andreasen & Powers, 1975)	15 creative writer, manic (n=16) and schizophrenic (n=15) patients.	Consecutive series of patients admitted to the University of Iowa Psychiatric Inpatient Service.	Writers from the University of Iowa Writers Workshop.	» Writers and manic patients showed more behavioral and conceptual overinclusion, but writers showed substantially more richness and the manic patients more idiosyncratic thinking. » Schizophrenic patients tended to be underinclusive rather than overinclusive and showed less richness and bizarreness than the writers and manic patients.

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(Dykes & Mcghie, 1976)	300 university students, 24 acute non-paranoid schizophrenic patients. From the 300 students the 24 highest scoring and the 24 lowest scoring subjects were extracted from the total group to represent our two extreme creativity groups.	Patients given a diagnosis of schizophrenia (made independently by two psychiatrists) and with an above-average verbal IQ.	Lovibond Object Sorting Test (divergent thinking), Chapman Card Sorting Test (convergent thinking), Dichotic Shadowing Task (assessing the degree to which each subject assimilates the information in both the relevant and irrelevant and the effect of the intrusion of irrelevant material on performance.	» Similarities in attentional strategies in creative and schizophrenic individuals, both groups appeared to sample a wider range of environmental input. » This widening of attention appeared to be involuntary in the schizophrenic, resulting in a deleterious effect on performance.
(al-Issa, 1976)	50 schizophrenics.	Patients were randomly selected from a hospital population and rated with the Activity-Withdrawal scale constructed by Venables and Epstein Inclusion Test.	10 tests for creative abilities as described by Guilford.	» Level of education and vocabulary are positively related to creativity scores, overinclusion, activity-withdrawal, and age tend to show the opposite trend.
(Kidner, 1976)	68 volunteers of British nationality.	Eysenck Psychoticism and Neuroticism scales, Raven's Advanced Progressive Matrices test and the Mill Hill Vocabulary test served as intelligence indices. Acceptance of Culture scale, was used as an index of socialization.	Wallach and Kogan's Object Uses, Similarities, and Pattern Meanings tests, scored for both fluency and originality.	» Creativity correlated positively with Eysenck's Psychoticism scale, and negatively with the Acceptance of Culture scale.
(Schou, 1979)	24 manic-depressive artists with lithium treatment were interviewed about their creative power during the treatment.	Manic-depressive illness, bipolar or unipolar, in whom prophylactic lithium treatment had been successful.	Artistic occupation.	» 12 artists reported increased artistic productivity, 6 unaltered productivity, and 6 lowered productivity.

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(Kauffman et al., 1979)	6 most competent children to 30 mothers with schizophrenia, bipolar or unipolar affective psychosis compared to 6 most competent children of mothers without any psychiatric disorder.	Anthony's six point scale. Ratings of maternal and paternal psychosocial functioning were based on the Strauss-Carpenter structured interview.	Anthony's six point scale. Ratings of maternal and paternal psychosocial functioning were based on the Strauss-Carpenter structured interview.	» The children from healthy families were not as creative as those in the high competence group of mothers with psychiatric disorders.
(Phillips, 1982)	8 patients with bipolar disorder receiving lithium treatment.	In clinical care by the author.	2 patients were artists.	» Impression that lithium maintenance treatment does not, in most instances, exert a negative influence on creativity.
(Tucker, Rothwell, Armstrong, & McConaghy, 1982)	74 final year students in high school.	Allusive (loose) thinking in Rapaport-Lovibond Object Sorting Test (OST).	Wallach & Kogantest, peer-rated creativity, assessment of creative activities, Holland Vocational Preference Inventory (VPI) Artistic Scale, Mill Hill Vocabulary Scale.	» When the effect of intelligence was accounted for, there was a relationship between peer-rated creativity and OST scores.
(Tucker et al., 1982)	Sydney's art galleries were asked to list 10 artists in Sydney whom they considered to be most creative. 12 artists accepted to participate.	Allusive (loose) thinking in Rapaport-Lovibond Object Sorting Test (OST).	The Kent-Rosanoff Word Association Test, Mill Hill Vocabulary Scale, Wallach & Kogan Creativity Test.	» Compared with administrators, visual artists had higher scores on OST.
(Rothenberg, 1983)	12 Nobel laureates (scientists), 18 hospitalized patients, and 113 college students.	Schizophrenia (2), borderline personality disorder (9), brief reactive psychosis (1), major depressive disorder (2), anorexia nervosa (1), opioid abuse (1), alcohol dependence (1), narcissistic personality disorder (1).	Students were divided into high (63) and low (50) creative groups on the basis of a quantitative assessment of their creative achievements in the arts and sciences. Each subject responded to 99 stimulus words. Word association responses were classified as opposite, primary, and other.	» Number of responses and speed of responses were sharply different within each creative group, and the group with proved creativity, the Nobel laureates, gave the highest number of opposite responses at the fastest rate of all groups. » The patient group did not show a tendency to rapid opposite responding.

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(Karlsson, 1984)	8007 relatives of psychotic persons born 1881-1910 were compared to the general population. The relatives were born 1851-1940.	1377 psychotic index patients admitted to the Kleppur Mental Hospital in Reykjavik, Iceland.	Graduates of the Reykjavik Gymnasium college, authors of published books or listed in the Who's Who	» The relatives were over-represented as graduates (2.5% vs 2.0%), authors (2.0% vs 1.3%), and in Who's Who (4.2% vs 3.4%).
(P. Kline & Cooper, 1986)	Healthy students (n=173; 96 females and 77 males).	Eysenck Personality Questionnaire	Scales from the Comprehensive Ability Battery (Flexibility of Closure, Spontaneous Flexibility, Ideational Fluency, Word Fluency, Originality)	» Only Word Fluency in males demonstrated a significant association.
(Shaw et al., 1986)	22 euthymic patients. The first, fourth and fifth week was with active lithium, whereas week two and three were with placebo.	DSM-III criteria: 20 patients who completed the protocol had bipolar disorder, 1 recurrent depressive disorder, 1 bipolar disorder (mixed). The patients had been receiving lithium therapy for a mean period of 9.4 years at mean lithium level of 0.80 mmol/liter.	Palermo and Jenkins' Word Association Norms. Associative idiosyncrasy or quality was measured by comparing the subject's associations to those norms. Words included by the patient that were not on the list were judged to be idiosyncratic.	» Lithium discontinuation produced a significant increase in associational productivity and a demonstrable increase in associative idiosyncrasy. Restoration of lithium dose significantly reversed both effects.
(N. C. Andreasen, 1987)	Rates of mental illness were examined in 30 creative writers (3 females, 27 males), 30 matched control subjects, and the first-degree relatives of both groups.	Structured interview designed by the. The probands were diagnosed according to the Research Diagnostic Criteria (RDC), and diagnoses of first-degree relatives were made according to the Family History Research Diagnostic Criteria.	The creative writers were drawn from a sample at the University of Iowa Writers' Workshop. A subset of 15 writers and control subjects: Raven Progressive Matrices and the WAIS.	<ul style="list-style-type: none"> <li>» 80% of the writers had had an episode of affective illness, compared with 30% of the control subjects.</li> <li>» 43% of the writers had had bipolar illness, compared with 10% of the controls.</li> <li>» Writers had higher rates of alcoholism (30%, compared with 7% in the controls).</li> </ul>

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(Richards et al., 1988)	17 manic-depressives, 16 cyclothymes, and 11 healthy first-degree relatives to patients were compared with 33 controls with no personal or family history of major affective disorder, cyclothymia, or schizophrenia; 15 controls were healthy and 18 carried another diagnosis.	DSM-III with primary or secondary diagnosis of manic-depressive illness. Controls having neither personal nor a family history of major affective disorder or cyclothymia, bipolar disorder, or schizophrenia or suicide.	Lifetime Creativity Scales.	<ul style="list-style-type: none"> <li>» Creativity significantly higher among the combined index subjects (manic-depressive, cyclothymes, and normal relatives) than among controls.</li> <li>» No significant difference between normal and ill controls.</li> <li>» Suggestively higher creativity among normal index relatives than among manic-depressives (<math>p &lt; .10</math>).</li> </ul>
(Schuldberg et al., 1988)	College students, who rated high on scales measuring schizotypy ( $n=52$ ; 23 females, 29 males) were compared with controls ( $n=65$ ; 32 females, 33 males).	The perceptual aberration scale, Magical ideation scale, Physical anhedonia scale, an infrequency scale. Subjects scoring $> 2$ SD on Perceptual aberration or Magical ideation. Controls scored max $\frac{1}{2}$ SDs above the mean.	The quick word test, Alternate uses test, Barron-Welsh art scale, ACL, and How do you think.	<ul style="list-style-type: none"> <li>» Association between schizotypal positive symptoms and the creativity tests.</li> <li>» This association was due to two tests: the Barron-Welsh art scale and How do you think.</li> </ul>
(K. R. Jamison, 1989)	Poets, playwrights, novelists, biographers and artists ( $n=47$ ).	Open-ended and scaled questions about history and type of treatment. Specific diagnostic criteria were not used.	Participants were selected on the basis of having won at least one prestigious prize.	<ul style="list-style-type: none"> <li>» 38% of the total sample had been treated for an affective illness.</li> <li>» The playwrights had the highest total rate of treatment for affective illness (63%).</li> <li>» Only poets (16.7%) were treated for bipolar illness with hospitalization, lithium, ECT, etc.</li> </ul>



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<p>(A. M. Ludwig, 1992)</p>	<p>1005 individuals.</p>	<p>ICD-9 based on biographic material.</p>	<p>Those whose biographies were reviewed in the New York Time Book Review 1960-1990. Creative Achievement Scale (CAS).</p>	<ul style="list-style-type: none"> <li>» Those in creative arts had higher rates of alcoholism, drug abuse, depression, mania, somatic problems, anxiety, psychoses, and adjustment disorders.</li> <li>» Theatrical professions demonstrated comparably high rates of alcohol and drug abuse, mania, anxiety disorders, and suicide attempts.</li> <li>» Writers of fiction and poets shared alcohol and drug abuse, depression, and suicide attempts.</li> <li>» Artists had comparably high rates of alcohol abuse, depression, anxiety, and adjustment problems.</li> <li>» Musical composers had especially heightened rates of alcohol abuse and depression.</li> </ul>
<p>(Post, 1994)</p>	<p>Family background, physical health, personality, psychosexuality, and mental health of 291 famous men in science, thought, politics, and art were investigated.</p>	<p>Based on biographies, extracted data were transformed into diagnoses in accordance with DSM-III-R criteria, when appropriate.</p>	<p>Subjects chosen were those judged to have achieved lasting international fame for their innovations in a variety of fields. Only biographies, which had been published sometime after the subjects' deaths were used.</p>	<ul style="list-style-type: none"> <li>» In general, these men were emotionally warm, with a gift for friendship and sociability.</li> <li>» Most had unusual personality characteristics and severe personality deviations were unduly frequent only in the case of visual artists (20%) and writers (25%).</li> <li>» Functional psychoses were entirely restricted to the affective varieties.</li> <li>» Among other disorders, only depressive conditions and alcoholism, were more prevalent and strikingly so in writers (72% resp. 14%).</li> </ul>

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<p>(A. M. Ludwig, 1994)</p>	<p>Questionnaire and interview data were obtained on 59 female writers and 59 members of a matched comparison group.</p>	<p>A series of standard inventories (e.g., Sensation-Seeking Scale, Rotter I-E Scale, Personal Reaction Inventory, Maudsley Personality Inventory, and Ways of Coping Checklist). Questionnaire for DSM-III-R criteria, in subjects and their biological parents and siblings.</p>	<p>Modified version Lifetime Creativity Scales and semi-structured Interviews.</p>	<ul style="list-style-type: none"> <li>» Writers were more likely to suffer from depression, bipolar disorder, drug abuse, panic attacks, generalized anxiety, eating disorders, and nonspecific emotional disorders.</li> <li>» The parents (in particular, the mothers) of the female writers were more likely to suffer from some sort of mental illness than those of the comparison group.</li> <li>» Higher percentages of writers than members of the comparison group reported experiencing sexual and physical abuse before the age of 13.</li> <li>» Writers were more likely than comparison subjects to identify their sexual orientations as homosexual or bisexual.</li> <li>» Writers displayed higher overall scores on the Lifetime Creativity Scales than the comparison group.</li> <li>» Marked creative activity in mothers, fathers, or any siblings resulted in an increased likelihood for a writer as a first-degree relative.</li> </ul>
<p>(Sitton &amp; Hughes, 1995)</p>	<p>14 men and 44 women in undergraduate psychology classes and from a local writers' organization (6 women, 2 men).</p>	<p>Beck depression inventory and a 16-item questionnaire dealing with atypical symptoms of depression, including seasonal variation in mood and productivity.</p>	<p>Remote Associates Test</p>	<ul style="list-style-type: none"> <li>» Fall was designated as the most productive season significantly more frequently than other seasons.</li> <li>» Failure to find a correlation between current depressive state and creativity.</li> </ul>

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(Sitton & Hughes, 1995)	College students (33 men and 67 women).	-	Brief questionnaire regarding perceptions of their creative processes, specifying any seasonal or daily variations in creativity. Thematic Apperception Test. Creativity of the stories was evaluated by judges.	<ul style="list-style-type: none"> <li>» No seasonal differences in the ratings of the stories.</li> <li>» Those who rated fall as their most creative season wrote stories rated as more creative than those who preferred spring regardless of the season in which they wrote.</li> </ul>
(Post, 1996)	~100 well-known American and British prose and play writers were included. Living poets and those who had died before the 1840s were excluded.	Based on biographies, extracted data were transformed into diagnoses in accordance with DSM-III-R criteria, when appropriate.	Anthologies of English (Gardner, 1972) and American (Ellmann, 1976) verse supplied the names of poets selected by experts.	<ul style="list-style-type: none"> <li>» Prevalence of dysfunctional personality traits (30%) was much higher than the 13% prevalence reported by Tyrer et al (1991) in a general population.</li> <li>» Psychopathology within the affective spectrum was found in 80.0% of poets, 80.5% of novelists/ poets, and in 87.5% of playwrights.</li> <li>» Eight writers committed suicide, and this 8% rate exceeded the 1980 rates of 0.73-0.84% for England and Wales as well as the 1.89-2.17 for Austria (World Health Organization, 1983).</li> <li>» Alcoholism was at its lowest in poets (31%) and highest in playwrights (54%).</li> <li>» The prevalence of bi- and homosexuality exceeded the population norm of 11.9% (Johnson et al, 1992) only in playwrights with 29%.</li> </ul>
(Karlsson, 1999)	Relatives of 1377 index cases with a psychotic diagnosis.	Admitted to a mental hospital.	The 6 best mathematics performers aged 20 each year during a 30-year period based on scores assigned in the mathematics examination at the Reykjavik College.	<ul style="list-style-type: none"> <li>» A 3% rate of hospitalization among the top mathematicians and their siblings.</li> <li>» There were 18 instances of psychosis instead of expected 5.</li> </ul>

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(Ghadirian, Gregoire, & Kosmidis, 2000)	20 patients with bipolar disorder and 24 patients suffering from other psychopathologies (schizophrenia, depression, and personality disorder) (23 females and 21 males).	Clinical diagnosis was established by a psychiatrist on the basis of DSM-III diagnostic criteria. All patients were assessed as: recovered, mildly ill, moderately ill, or severely ill.	A battery of tests measuring creativity in nonverbal, visual-motor, perceptual, and verbal subtests.	» There was no significant difference in creativity between the two groups with bipolar disorder and other psychopathologies, respectively. » The group of patients identified as severely ill showed significantly lower levels of creativity, than the three other groups.
(Kinney et al., 2000)	36 adult adoptees of biological parents with schizophrenia, and 36 control adoptees with no biological family history of psychiatric hospitalization.	DSM-III, based on structured interview.	Lifetime Creativity Scales	» Non-schizophrenics with either schizotypal or schizoid personality disorder or multiple schizotypal signs had significantly higher creativity than other participants.
(Weinstein & Graves, 2002)	60 undergraduates. 21 men (3 non-right-handed) and 39 women (4 were non-right-handed).	Edinburgh Handedness Inventory, Magical Ideation, Perceptual Aberration, Revised Social Anhedonia, 13 infrequency items. Stimuli for the lexical decision task were 15 four-letter English words and 45 four-letter nonsense words. The dichotic listening task (DLT) stimuli were six natural voice, consonant-vowel (CV) nonsense syllables produced.	Shortened version of the Remote Associates Test, Thurstone Written Fluency Test.	» Creativity and schizotypy (per-mag) are correlated. » Creativity and schizotypy (per-mag) are partly related to a response criterion favoring right hemisphere. » Dichotic listening results revealed a strong association of better right hemisphere (left ear) localization ability and creativity.
(Papworth & James, 2003)	104 undergraduate students (N=36 art and 68 science)	Depression Adjective Check List, Cognitive Distortion Questionnaire.	Torrance Tests of Creative Thinking, Means-Ends Problem Solving Procedure	» Art students were found to be more creative, experienced lower mood, and displayed greater degrees of distortion and bias in their appraisals.

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(Ramey & Weisberg, 2004)	Emily Dickinson's creative productivity over the course of her career was examined to test the hypothesis that mood disorder affects creative thinking.	-	Franklin's (1998) collection of Dickinson's poetry was used to determine the date of each of Dickinson's poems. 19 anthologies of poetry and tabulated the number of Dickinson's poems that were present in each to investigate quality.	» During the years with Seasonal affective disorder, a significant increase was found in quality of poems produced during autumn + winter. This relationship did not hold for the hypomanic years.
(Nowakowska, Strong, Santosa, Wang, & Ketter, 2005)	49 bipolar patients (BP), 25 with major depressive disorder (MDD), 32 creative controls (CC), and 47 healthy controls (HC) completed self-report temperament/personality measures.	Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS-A), NEO-PI-R, and the Temperament and Character Inventory (TCI). Structured Clinical Interview (SCID) for DSM-IV Diagnosis was conducted by a psychiatrist or experienced research coordinator to determine presence or absence of psychiatric disorders, and confirm euthymic mood state.	CC's were volunteers with no current psychiatric or substance abuse problems, recruited from graduate programs in creative writing, fine arts, and product design at Stanford University.	<ul style="list-style-type: none"> <li>» Euthymic BP, MDD, and CC, compared to HC, had significantly increased cyclothymia, dysthymia and irritability scores on TEMPS-A; increased neuroticism and decreased conscientiousness on NEO-PI-R; and increased harm avoidance and novelty seeking as well as decreased self-directedness on TCI.</li> <li>» TEMPS-A cyclothymia scores were significantly higher in BP than in MDD.</li> <li>» NEO-PI-R openness was increased in BP and CC, compared to HC, and in CC compared to MDD.</li> <li>» TCI self-transcendence scores in BP were significantly higher than in MDD, CC, and HC.</li> </ul>
(Schulberg, 2005)	625 undergraduate students.	Eysenck Personality Questionnaire, Wisconsin scales of hypothetical Psychosis-proneness and Hypomanic traits, the Golden and Meehl Schizoid taxon scale.	Alternate uses, Revised Art Scale, How Do You Think, Gough's Adjective Checklist creativity scale, Remote Associates Test.	<ul style="list-style-type: none"> <li>» The Psychoticism scores were correlated (.30) with Hypomanic traits, (.25) with Perceptual Aberration, and (.20) with the How Do You Think.</li> <li>» Psychoticism scores were negatively related to Remote Associates Test.</li> <li>» Extraversion scores were correlated (.45) with How Do You Think, and (.37) with Adjective Checklist.</li> </ul>

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(Simeonova et al., 2005)	40 adults with bipolar disorder (BD), 20 bipolar offspring with BD, 20 bipolar offspring with ADHD, and 18 healthy control parents and their 18 healthy control children.	Structured Clinical Interview for DSM-IV Axis I Disorders (SCID), Family History-Research Diagnostic Criteria (FH-RDC), WASH-U-KSADS, K-SADS-PL, YMRS, CDRS-R. All evaluations were conducted by either a child and adolescent psychiatrist or a master level research assistant.	Barron-Welsh Art Scale (BWAS)	<ul style="list-style-type: none"> <li>» Adults with BD compared to controls scored (120%) higher on the BWAS Dislike subscale, and non-significantly (32%) higher on the BWAS Total scale.</li> <li>» Mean BWAS Dislike subscale scores were higher in offspring with BD (107% higher) and offspring with ADHD (91% higher) than in healthy control children.</li> <li>» In the bipolar offspring with BD, BWAS Total scores were negatively correlated with duration of illness.</li> </ul>
(Folley & Park, 2005)	17 outpatient schizophrenic (SZ) subjects. 17 healthy control (CO) and 17 schizotypal (SCT). 10 SZ, 10 SCT and 10 CO participated in near-infrared optical spectroscopy (NIRS) part of the study.	DSM-IV. Brief Psychiatric Rating Scale (BPRS), Scales for the Assessment of Positive (SAPS) and Negative (SANS) Symptoms, Schizotypal Personality Questionnaire (SPQ), Wechsler Abbreviated Scales of Intelligence, Edinburgh Handedness Inventory. NIRS was performed using a 24-channel spectrometer.	Remote Associates Test (RAT) and a novel divergent thinking task (DT) based on earlier models of creativity. Fluency was measured using verbal (FAS) category, and design (Five Point Test) fluency tasks.	<ul style="list-style-type: none"> <li>» CO gave more correct responses than schizophrenics on the RAT.</li> <li>» SCT had enhanced DT ability compared with SZ and CO, who showed similar performance overall.</li> <li>» NIRS data showed that DT was associated with bilateral prefrontal cortex (PFC) activation, but the right PFC particularly contributed to the enhanced creative thinking in SCT compared with the other two groups.</li> </ul>
(Nettle & Clegg, 2006)	425 British adults (156 male, 269 female).	O-LIFE schizotypy inventory and a section on psychiatric history and information on mating success ('Since you were 18, how much of the time have you been in a steady relationship?' and 'Since you were 18, how many different partners have you?').	Participants indicated their degree of creative activity in poetry or visual art. Participants rated themselves as not producing poetry or art (241 participants), being a hobby producer (57), a serious producer (60) or a professional producer (67) in either domain.	<ul style="list-style-type: none"> <li>» Positive relationships between <i>unusual experiences</i> and mating success, and <i>impulsive non-conformity</i> and mating success.</li> <li>» In <i>unusual experiences</i>, this relationship was mediated by creative activity.</li> <li>» In <i>impulsive non-conformity</i>, this relationship was not mediated by creative activity.</li> <li>» <i>Introverted anhedonia</i> decreased creative activity, and also had a direct negative effect on mating success.</li> </ul>

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(Nettle, 2006)	501 individuals (309 healthy, 168 affective disorder, 13 schizophrenia, 11 bipolar disorder).	Psychopathology was rated from answers to detailed questions about symptoms and treatment. O-LIFE schizotypy.	Poets, visual artists, mathematicians.	<ul style="list-style-type: none"> <li>» Poets and artists had levels of <i>unusual experiences</i> that were higher than controls, and as high as schizophrenia patients. However, they were relatively low on the dimension of <i>introverted anhedonia</i>.</li> <li>» Mathematicians were lower than controls on <i>unusual experiences</i>.</li> </ul>
(Burch et al., 2006)	107 undergraduate and postgraduate students.	O-LIFE, NEO-FFI, Wechsler abbreviated scale of intelligence	53 students were recruited from the Department of Visual Arts. Remaining 54 participants were all non-artists. Creative personality scale, Instances and Uses tests of divergent thinking.	<ul style="list-style-type: none"> <li>» Largest difference between the visual artists and non-artists occurred on <i>unusual experience</i> scores of the O-LIFE.</li> <li>» Visual artists scored higher than non-artists on cognitive disorganization, impulsive nonconformity, neuroticism, openness and divergent thinking (uniqueness), while non-artists scored higher on agreeableness.</li> <li>» Males generally scored higher on both divergent thinking uniqueness and totals scores, IQ and impulsive nonconformity scores.</li> </ul>
(Abraham et al., 2007)	28 patients with schizophrenia (SZ) and 18 healthy controls.	Schedules for assessment of positive and negative symptoms (SAPS and SANS) of the Comprehensive Assessment of Symptoms and History (CASH). Digit backward span, Hayling sentence completion test, Brixton spatial anticipation test, Stroop Neuropsychological Screening Test.	Ward animal task, Creative imagery, Constraints of examples, Alternate uses, Convergent (insight and incremental) problem solving.	<ul style="list-style-type: none"> <li>» In executive function measures, except Hayling task on which no significant difference in performance was found between the groups, SZ had poorer performance than the control group on all the other executive tasks.</li> <li>» In creative cognition measures, SZ were poorer in performance on insight problem, incremental problem, imagery measure, alternate uses uniqueness, and the alternate uses fluency.</li> </ul>

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<p>(Santosa et al., 2007)</p>	<p>49 patients with bipolar disorder (BP), 25 Major depressive disorder (MDD), 32 creative controls (CC), and 47 healthy controls (HC) (all euthymic).</p>	<p>Medical and psychiatric history and Structured Clinical Interview for DSM-IV Diagnosis (SCID) by a psychiatrist or experienced research coordinator. Psychiatrist utilizing a semi-structured interview confirmed that subjects were euthymic.</p>	<p>Barron-Welsh Art Scale (BWAS), the Adjective Check List Creative Personality Scale, and the Torrance Tests of Creative Thinking – Figural (TTCT-F) and Verbal versions.</p>	<p>» BP and CC (but not MDD) compared to HC scored significantly higher on BWAS Total and BWAS Dislike, but not on BWAS Like.                  » CC compared to MDD scored significantly higher on TTCT-F.</p>
<p>(Strong et al., 2007)</p>	<p>49 patients with bipolar disorder, 25 Major depressive disorder, 32 creative controls, and 47 healthy controls (all euthymic).</p>	<p>Medical and psychiatric history and Structured Clinical Interview for DSM-IV Diagnosis (SCID) by a psychiatrist or experienced research coordinator. Psychiatrist utilizing a semi-structured interview confirmed that subjects were euthymic. Revised NEO Personality Inventory (NEO-PI-R), the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A), and the Temperament and Character Inventory (TCI).</p>	<p>Barron-Welsh Art Scale (BWAS), the Adjective Check List Creative Personality Scale, and the Torrance Tests of Creative Thinking – Figural (TTCT-F) and Verbal versions.</p>	<p>» Neuroticism/Cyclothymia/Dysthymia Factor, comprised mostly of NEO-PI-R-Neuroticism and TEMPS-A-Cyclothymia and TEMPS-A-Dysthymia, was related to BWAS Total scores and BWAS Dislike subscale scores.                  » An Openness Factor, comprised mostly of NEO-PI-R-Openness, was related to BWAS Like subscale scores, and to ACL-CPS scores.</p>



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<p>(G. F. Miller &amp; Tal, 2007)</p>	<p>225 University of New Mexico students.</p>	<p>Schizotypy (SPQ), NEO-FFI, Raven's Advanced Progressive Matrices. Family psychiatric history was assessed by participants checking presence or absence of 25 possible DSMIV-TR mental illnesses 'that you know have affected any members of your family'.</p>	<p>6 verbal creativity tasks and 8 drawing creativity tasks.</p>	<ul style="list-style-type: none"> <li>» Two factors were obtained: a 'positive schizotypy'; and a 'negative schizotypy' factor.</li> <li>» Only intelligence (Raven) and openness (NEO-FFI) predicted verbal creativity in multiple regression.</li> <li>» Openness predicted drawing creativity even more strongly than it predicts verbal creativity, whereas intelligence predicted drawing creativity significantly, but less strongly than it predicted verbal creativity in multiple regression.</li> <li>» Self-reported capacities to be creative, inventive, imaginative, interesting, entertaining, funny, and witty were slightly correlated with positive schizotypy.</li> <li>» Drawing creativity was positively predicted by the family mood/anxiety/personality disorders factor, and negatively predicted by the family impulse control disorders factor.</li> </ul>
<p>(Preti &amp; Vellante, 2007)</p>	<p>80 creative artists (CA) and 80 noncreative controls.</p>	<p>Annett Hand Preference Questionnaire, Peters et al. Delusions Inventory, General Health Questionnaire.</p>	<p>30 musicians, 25 painters, and 25 writers.</p>	<ul style="list-style-type: none"> <li>» CA were more likely to use the left hand, with more left hand use reported by artists involved in music and painting.</li> <li>» CA scored higher on the Peters et al. Delusions Inventory.</li> <li>» CA were more likely to have experienced both licit and illicit psychotropic substances.</li> </ul>
<p>(Forgeard, 2008)</p>	<p>30 authors (10 bipolar disorder, 10 unipolar depression, 10 controls).</p>	<p>Retrospective on biographies.</p>	<p>Linguistic Inquiry and Word Count.</p>	<ul style="list-style-type: none"> <li>» Bipolar writers referred to death more than did unipolar writers.</li> <li>» Unipolar writers referred to people other than themselves more than did control writers.</li> <li>» Unipolar writers used more words describing cognitive mechanisms (e.g., understand, know) than did both other groups.</li> </ul>

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(Nelson & Rawlings, 2008)	100 artists (57 females, 43 males).	Big Five Inventory, Unusual Experiences Questionnaire from O-LIFE, Boundary Questionnaire, General Behavior Inventory.	Experience of Creativity Questionnaire (ECQ).	» Schizotypy (O-LIFE) displayed correlations with all the ECQ scales, apart from Clarity/Preparation.
(Claridge & McDonald, 2009)	77 university students (44 females, 33 males).	O-LIFE, AQ.	Sub-tests from the Wallach-Kogan divergent thinking test, two convergent thinking tasks: Missionaries and Cannibals, and Tower of Hanoi.	» Suggested relationships between negative schizotypy, autistic traits, and convergent thinking. » Expected association between positive schizotypy and divergent thinking was not replicated.
(Murphy, 2009)	Salvador Dalí.	Presence of psychotic disorder (OPCRIT) and personality disorder questionnaire (PDQ-R), retrospectively.	-	» Dalí was found to meet the diagnostic criteria for several DSM Cluster A and Cluster B personality disorders, as well as for psychotic illnesses.
(Keri, 2009)	200 healthy participants with high intellectual and academic performance. Another 128 participants provided population means for creative tests.	Structured Clinical Interview for DSM-IV, IQ (Wechsler, 1981), and schizotypal traits (SPQ). Genotyping was performed for single-nucleotide polymorphisms of the Neuregulin 1 gene.	Creative Achievement Questionnaire (CAQ) and the 'Just Suppose' subtest of the Torrance Test of Creative Thinking (TTCT).	» Neuregulin 1 gene (SNP8NRG243177/rs6994992) is associated with CAQ and TTCT. » Highest creative achievements and creative thinking scores were found in people who carried the T/T genotype, previously shown related to psychosis risk.
(Tremblay, Grosskopf, & Yang, 2010)	84 individuals in the sample with information on occupation who have a DSM-III manic episode diagnosis (46 with inpatient treatment).	NIMH Diagnostic Interview Schedule (DIS) for DSM-III. DIS responses were entered into a computer.	Creative occupation.	» Those with bipolar illness appear to be disproportionately concentrated in the most creative occupational category.

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(Srivastava et al., 2010)	32 bipolar disorder patients (BP), 21 unipolar major depressive disorder patients (MDD), 22 creative controls (CC), and 42 healthy controls (HC) (all euthymic).	Revised Neuroticism Extraversion Openness Personality Inventory (NEO), the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A), the Myers-Briggs Type Inventory (MBTI).	Barron-Welsh Art Scale (BWAS), the Adjective Check List Creative Personality Scale (ACL), and the Figural and Verbal Torrance Tests of Creative Thinking (TTCT).	<ul style="list-style-type: none"> <li>» BP and CC (but not MDD) compared to HC had higher BWAS Total and BWAS Dislike scores, and higher MBTI-Intuition preference type rates.</li> <li>» BP, MDD, and CC, compared to HC, had increased TEMPS-A-Cyclothymia scores, and NEO-Neuroticism scores.</li> <li>» NEO-Neuroticism and TEMPS-A Cyclothymia correlated with BWAS Dislike (and BWAS Total).</li> <li>» MBTI-Intuition continuous scores and NEO-Openness correlated with BWAS Like (and BWAS Total).</li> </ul>
(Rybakowski & Klonowska, 2011)	40 patients with bipolar disorder (BP), and 48 controls.	ICD-10 and DSM-IV criteria. Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS), Schizotypy (O-LIFE).	Revised Art Scale (RAS) based on Barron-Welsh Art Scale, test battery 'inventiveness' of the Berlin Intelligence Structure Test (BIS)	<ul style="list-style-type: none"> <li>» BP better results on the total creativity BIS scale and also on a BIS subscale of verbal creativity.</li> <li>» Detrimental effect of depression on creativity measured by the BIS scale.</li> <li>» In BP, the total O-LIFE correlated with RAS-like, RAS-dislike and RAS total.</li> <li>» Impulsive Nonconformity in O-LIFE correlated with BIS.</li> </ul>
(Kyaga et al., 2011)	54 042 people with schizophrenia (SZ), 29 644 people with bipolar disorder (BP) and 217 771 people with unipolar depression (UD). First-, second-, and third-degree relatives of these individuals were also included. Ten matched controls for each person in the case group and each of their.	ICD8-10.	Creative professions (artistic and scientific).	<ul style="list-style-type: none"> <li>» Individuals with BP and healthy siblings of people with SZ or BP were over-represented in creative professions.</li> <li>» People with schizophrenia had no increased rate of overall creative professions compared with controls, but an increased rate in the subgroup of artistic occupations.</li> </ul>

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(Soeiro-de-Souza, Dias, Bio, Post, & Moreno, 2011)	67 bipolar type I patients. 20 patients were experiencing manic episodes; 21 mixed states and 26 depressive episodes.	Structured Clinical Interview (SCID-I/P) for DSM-IV TR. The Young Mania Rating Scale (YMRS), and the Montgomery–Asberg Depression Rating Scale (MADRS), Clinical Global Impression scale, Wisconsin Card Sorting Test (WCST), Wechsler Abbreviated Scale of Intelligence (WASI).	Barrow-Welsh Art Scale (BWAS).	<ul style="list-style-type: none"> <li>» Manic and mixed state patients had higher creativity scores than depressive individuals.</li> <li>» Creativity was influenced by executive function measures only in manic patients.</li> <li>» Intelligence did not influence creativity for any of the mood episode types.</li> </ul>
(Vellante et al., 2011)	152 undergraduate creative students and 152 students in areas mainly requiring application of learned rules.	TEMPS-A (Temperament Evaluation of the Memphis, Pisa, Paris and San Diego — Autoquestionnaire), the General Health Questionnaire (GHQ).	Creative Achievement Questionnaire (CAQ).	<ul style="list-style-type: none"> <li>» Creative people scored higher than controls on the CAQ and on the cyclothymic, hyperthymic and irritable subscales of the TEMPS-A.</li> <li>» CAQ was positively associated with cyclothymic and hyperthymic, and partly with irritable subscales of the TEMPS-A.</li> </ul>
(Fink, Slamar-Halbedl, Unterrainer, & Weiss, 2012)	69 participants (18 alcohol dependents, 18 polysubstance dependents, 21 university students, 17 actors).	Eysenck's Personality Questionnaire, Brief Symptom Inventory, Wonderlic Personnel Test, Latent inhibition (LI).	Berliner Intelligenz Struktur Test, Picture Completion subtest of the Torrance Tests of Creative Thinking.	<ul style="list-style-type: none"> <li>» Actors and polydrug dependents had high scores on psychoticism, high originality during creative idea generation, and decreased LI as compared with the other groups.</li> <li>» Associations between LI, originality, and psychoticism were found.</li> </ul>

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<p>(Soeiro-de-Souza et al., 2012)</p>	<p>66 medication-free subjects with bipolar disorder (41 in manic and 25 in depressive episodes) and 78 healthy controls.</p>	<p>Diagnosis was determined by psychiatrists using the Structured Clinical Interview (SCID-I) for DSM-IV TR. Mini International Neuropsychiatric Interview, Young Mania Rating Scale, Montgomery-Asberg Depression Rating Scale, neurocognitive tests for attention, verbal memory, visuospatial function, language, psychomotor speed, executive function, and intelligence. Genotyped for BDNF Val66Met.</p>	<p>Barrow-Welsh Art Scale (BWAS).</p>	<ul style="list-style-type: none"> <li>» Manic patients with the Val allele (Met-) had higher BWAS scores than Met+ carriers.</li> <li>» This relationship was not observed among patients in depressive episodes or among control subjects.</li> </ul>
<p>(Kyaga et al., 2012)</p>	<p>1173763 patients with schizophrenia, schizoaffective disorder, bipolar disorder, unipolar depression, anxiety disorders, alcohol abuse, drug abuse, autism, ADHD, anorexia nervosa, and completed suicide. First-, second-, and third-degree relatives of these individuals were also included. Ten matched controls for each person in the case group and each of their relatives.</p>	<p>ICD8-10.</p>	<p>Creative professions (artistic and scientific).</p>	<ul style="list-style-type: none"> <li>» Except for bipolar disorder, individuals with overall creative professions were not more likely to suffer from investigated psychiatric disorders than controls.</li> <li>» Authors were specifically associated with increased likelihood of schizophrenia, bipolar disorder, unipolar depression, anxiety disorders, substance abuse, and suicide.</li> <li>» There was an association between overall creative professions and first-degree relatives of patients with schizophrenia, bipolar disorder, anorexia nervosa, and for siblings of patients with autism.</li> </ul>

(Young, Winner, & Cordes, 2013)	2482 15- to 16-year-old adolescents.	Center for Epidemiological Studies Depression Scale (CES-D).	Amount of involvement in arts and sports in the time period after school, verbal IQ (Peabody Picture Vocabulary Test-Revised), working memory (Wechsler Intelligence Scales for Children-Revised).	<ul style="list-style-type: none"> <li>» Teens involved in after-school arts had higher depressive symptom scores than those not involved.</li> <li>» The association between arts involvement and depressive symptoms held only for those scoring above the median in working memory.</li> </ul>
(Jaracz et al., 2012)	43 patients with paranoid schizophrenia in symptomatic remission and 45 healthy controls.	A consensus diagnosis of paranoid schizophrenia was made for each patient, by at least two psychiatrists, according to DSM-IV criteria. Patients with a total positive and negative symptoms scale (PANSS) score of less than 60 were included.	Barron-Welsh Art Scale (BWAS) and the inventiveness part of the Berlin Intelligence Structure Test (BIS). Executive functions were measured by means of the Wisconsin Card Sorting Test (WCST).	<ul style="list-style-type: none"> <li>» Patients gave responses on the BWAS, had lower total score on the BIS and in the figural test, and performed worse on all domains of the WCST compared with controls.</li> <li>» Their lower scores on the BIS correlated with lower scores on the WCST.</li> </ul>

#### 1.2.4 Neurodevelopmental disorders

Although far fewer studies have examined neurodevelopmental disorders than psychotic and mood disorders in relation to creativity, there has been a substantial interest in whether young patients with these disorders have creative abilities surpassing their peers. Most studies have investigated learning disabled children and students. More recently, focus has turned to ADHD/ADD and possible effects of medication in these disorders.

##### 1.2.4.1 *Autism spectrum disorders*

Turner investigated individuals aged 6-32 years who were high-functioning (IQ>75) with autism (n=22), high-functioning controls (n=22), autistic (n=22), and learning disabled controls (n=22) (1999). Subjects with autism generally showed reduced fluency for both words and ideation. Another study by Pring et al. explored 9 savant artists with autism spectrum disorder (SASD), 9 non-talented comparison adults with autism spectrum disorder (ASD), 9 non-talented adults with mild/moderate learning difficulties (MLD), and 9 artistically talented students (2012). Results showed that the art students performed better than the other three groups on the Torrance Test of Creative Thinking, while SASD produced more elaborate responses than the ASD and

MLD groups on a drawing task. On the non-drawing construction task, SASD produced more original outputs than the ASD, MLD and art student groups. Campbell et al. made an online survey of an incoming class to Princeton University and demonstrated that students aspiring to *technical majors* were more likely than other students to report a sibling with ASD (2012).

#### 1.2.4.2 ADHD/ADD

In line with the rising awareness on ADHD/ADD, some authors have also investigated whether there is any connection between ADHD/ADD and creative abilities. Funk et al. examined 19 boys with previously diagnosed ADHD and 21 comparison boys aged 8 through 11 on two administrations of tests of creativity (1993). Boys with ADHD received prescribed methylphenidate only for the first session. Creativity scores for comparison boys were somewhat higher than for boys with ADHD. No changes in performance over medication state were observed. Healey et al. similarly investigated 67 children, ages 10 to 12 (33 patients with ADHD unmedicated for 24hr, and 34 controls), revealing no significant difference between the ADHD group's and control group's performance on creativity scores (2005). In a follow-up study, Healey et al. demonstrated that 40 percent of a sample of creative children displayed ADHD symptomatology, but none met full criteria for ADHD (2006). Abraham et al. showed that ADHD patients exhibited a reduced capacity to generate a functional invention during an imagery task (2006). White et al. on the other hand, demonstrated in two studies that university undergraduates with ADHD scored higher on both divergent thinking measures and creative achievements (2006, 2011). Similarly, in the previously mentioned study by Simeonova et al. the mean creativity scores assessed by the BWAS Dislike subscale were also higher in a subgroup of offspring to patients with bipolar disorder diagnosed with ADHD compared to healthy control children (2005).

#### 1.2.4.3 Learning disability disorders

Studies of creativity in individuals with learning disability disorders have a somewhat longer history, than for ADHD/ADD. Argulewicz investigated 39 elementary grade children with learning disability in 1979 (1979). The children scored in the same range as average children on all constructs of creativity except *elaboration*. On this component they scored significantly below average. Similar results were found by Sigg et al. and Graham et al., who found that the children with learning disability disorders scored similar or below average on different aspects of creativity (Graham & Sheinker, 1980; Sigg & Gargiulo, 1980). Eisen on the other hand demonstrated increased performance of 16 children with learning disabilities administered a non-verbal creativity

task compared to controls (1989). The author also reported a negative correlation between the verbal and nonverbal tests, suggesting that there is a link between the verbal deficits and the creative style of children with learning disabilities.

TABLE 2. SUMMARY OF STUDIES PRIMARILY INVESTIGATING NEURODEVELOPMENTAL DISORDERS

REFERENCE	STUDY SAMPLE	ASSESSMENT OF MENTAL DISORDER	DEFINITION OF CREATIVITY	FINDINGS
(Argulewicz et al., 1979)	39 elementary grade children.	Diagnosed as learning disabled.	Torrance Tests of Creative Thinking, Figural form A.	» Scored in the same range as average children on all constructs of creativity except elaboration. On this component they scored below average.
(Sigg & Gargiulo, 1980)	42 learning disabled and 44 nondisabled students. Mean chronological age for the learning disabled students was 9.4 and 8.8 for nondisabled learners.	Handicapped learners were chosen from self-contained special education classrooms.	Matching Familiar Figures Test and the Torrance Test of Creative Thinking.	» Learning disabled and nondisabled students did not significantly differ in their performance on the Torrance measures of creative thinking.
(Graham & Sheinker, 1980)	26 learning-disabled and 30 average students in grades 3, 4, and 5.	Learning-disabled students were receiving services in a program for perceptual communication.	Figural Form A of the Torrance Tests of Creative Thinking and Sounds and Images, containing a series of free-association tasks designed to measure originality.	» Learning-disabled and average students produced equivalent numbers of relevant responses on nonverbal measures of creativity. » Learning-disabled students were less able to generate new ideas and change an initial approach.
(Eisen, 1989)	Sixteen normally performing and 16 children with learning disabilities (LD) were administered a non-verbal creativity task and a control task of verbal fluency. The age of the subjects ranged from 8 years, 5 months to 11 years, 11 months.	All the LD students had been diagnosed by the Chicago public school system.	Assorted geometric shapes were used as test items. The subjects were asked to create pictures from these shapes. These pictures were in turn scored on their originality, remoteness, and fluency.	» Children with LD scored higher on the nonverbal but not the verbal control task. » Increased performances of children with learning disabilities were found in remoteness, originality, and number of pieces per picture.



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(Funk et al., 1993)	19 boys with ADHD and 21 comparison boys aged 8 through 11. Boys with ADHD received prescribed methylphenidate only for the first session.	ADHD must have been previously determined by physician or multidisciplinary team diagnosis, the child must have been currently receiving methylphenidate therapy, and there must have been elevations in Conners' Hyperactivity Index score by parent report.	Alternate forms of the Torrance Tests of Creative Thinking-Figural (nonverbal). Two administrations of tests of creativity.	<ul style="list-style-type: none"> <li>» Mean Torrance summary scores for comparison boys were higher than for boys with ADHD.</li> <li>» No changes in performance over medication state (ADHD group) were observed.</li> </ul>
(Turner, 1999)	Four groups of subjects: high-functioning (IQ>75) with autism (n=22), high-functioning controls (n=22), autism (n=22), learning disabled controls (n=22). Subjects were aged 6–32 years.	Diagnoses were verified at the time of the study through two interviews administered incorporating diagnostic criteria for autism outlined in the DSM-III-R.	Letter fluency task, Category fluency task, Uses of objects task, Pattern meaning task, Design fluency task	<ul style="list-style-type: none"> <li>» Subjects with autism showed reduced fluency for both word and ideational fluency tasks.</li> <li>» The design fluency paradigm revealed no significant difference in the quantity of designs generated, but a clear qualitative difference. The autistic group produced higher rates of disallowed and perseverative responses.</li> </ul>
(Healey & Rucklidge, 2005)	67 children, ages 10 to 12 (33 ADHD and 34 controls). 30 of ADHD children were taking medication (methylphenidate). They were asked not to take it 24 hrs prior to the day of testing.	ADHD was diagnosed by a psychiatrist or registered psychologist. Parent and teacher forms of the Conners' Rating Scales-Revised.	Torrance Tests of Creative Thinking (TTCT) Figural form A, Maier's Two-String Problem, and the Block Design and Vocabulary subsets of the Wechsler Intelligence Scale for Children (WISC-III).	<ul style="list-style-type: none"> <li>» No significant difference between the ADHD group's and control group's performance on either the TTCT, Maier's Two-String Problem, or WISC-III.</li> </ul>
(Abraham et al., 2006)	11 ADHD (3 girls, 8 boys) patients, 12 patients with conduct disorder (CD) (4 girls, 8 boys), and a control group of 21 children (9 girls, 12 boys) who had no history of mental illness.	3 IQ subscales (Verbal Factor, Reasoning, and Closure) from the Leistungsprüfungssystem. Patients were diagnosed using DSM-IV and recruited with the guidance of the chief consultant psychiatrist from a local Child and Adolescent Psychiatry Unit.	Conceptual expansion task, the recently activated knowledge task, the creative imagery task, and the alternate uses task.	<ul style="list-style-type: none"> <li>» The ADHD group exhibited an enhanced ability in overcoming the constraining influence of examples, but a reduced capacity to generate a functional invention during the imagery task.</li> <li>» The CD group exhibited poorer performance on the originality component of the creative imagery task in comparison to the control group.</li> </ul>

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(Healey & Rucklidge, 2006)	29 ADHD children without creativity, 12 creative children (CC) with ADHD symptoms, 18 creative children without ADHD symptoms, and 30 controls.	Parent form of the Conners' Rating Scales-Revised (CPRS-R), K-SADS-PL, Wechsler intelligence scale for children (WISC-III), Rapid Automatized Naming (RAN), Stop task tracking version, Stroop Task, Stroop negative priming task, Tower of London.	Torrance Tests of Creative Thinking (TTCT), Maier's two-string problem.	» 40% of CC displayed ADHD symptomatology, but none met full criteria for ADHD.
(White & Shah, 2006)	90 university undergraduates (45 ADHD; mean age 19.4 years, 45 controls; mean age 19.5 years).	DSM-IV, Current Symptoms and Childhood Symptoms Scales, Boatwright-Bracken Adult Attention Deficit Disorder Scale. No medication within two weeks prior to participation.	Remote Associates Test, Unusual Uses Task, Semantic Inhibition of Return Task.	» ADHD individuals outperformed non-ADHD individuals on the Unusual Uses Task. » ADHD individuals performed worse than non-ADHD on the Remote Associates Test and the semantic IOR task.
(Wei, 2011)	127 children with Tourette's Syndrome (TS; 21 females, 106 males; 6 to 12 years) and 138 controls.	DSM-IV criteria, parents' questionnaire of 'School and Family Adjustment'.	Williams' Creativity Assessment Packet of Divergent Thinking Test.	» TS had significantly lower scores on Elaboration in the creativity assessment.
(White & Shah, 2011)	60 university undergraduates (30 ADHD, 30 controls).	DSM-IV, Current Symptoms and Childhood Symptoms Scales, Conners' adult ADHD rating scale. One half of the ADHD group was taking medication to treat ADHD.	Creative Achievement Questionnaire, FourSight Thinking Profile, Abbreviated Torrance Test for Adults.	» Higher overall creative achievement in the ADHD group. » Adults with ADHD produced more original responses on the verbal component of the Abbreviated Torrance Test for Adults (ATTA).
(Campbell & Wang, 2012)	Online survey of incoming class of 2014 at Princeton University (n=1077).	Question: 'Do you have a sibling with autism spectrum disorder (ASD)?' ASD includes autism, Asperger's, and pervasive developmental disorder not otherwise specified.	527 technical major (natural sciences, engineering, or mathematics), 394 nontechnical majors (245 in social sciences, 149 in humanities), and 156 students were undecided.	» Students aspiring to technical majors were more likely than other students to report a sibling with ASD. » Students interested in the humanities were more likely to report a family member with major depressive, bipolar disorder, or substance abuse problems.

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(Pring et al., 2012)	9 savant artists with autism spectrum disorder (SASD), 9 non-talented comparison adults with autism spectrum disorder (ASD), 9 non-talented adults with mild/moderate learning Difficulties (MLD), and 9 artistically talented students.	Peabody Picture Vocabulary Test (PPVT), Raven's Standard Progressive Matrices or Coloured Progressive Matrices.	Incomplete and repeated figures tasks of the Torrance Test of Creative Thinking (TTCT), figural synthesis task (FST).	<ul style="list-style-type: none"> <li>» On the TTCT, the art students performed significantly better than the other three groups.</li> <li>» SASD produced more elaborate responses than the ASD and MLD groups.</li> <li>» On the non-drawing construction task, SASD produced more original outputs than the ASD, MLD and art student groups.</li> </ul>
(Jolley, O'Kelly, Barlow, & Jarrold, 2013)	60 5-19-year-olds (15 with non-savant autism (AUT) and the others with learning difficulty, similar mental age or similar chronological age.	Diagnosed by a fully qualified clinical psychologist according to the DSM criteria.	Happy and sad drawings were requested.	<ul style="list-style-type: none"> <li>» AUT did not draw fewer people, but more immature forms than mental age controls.</li> <li>» There was tentative evidence that fewer social scenes were produced by AUT.</li> </ul>
(Hobson, Hobson, Malik, Bargiota, & Calo, 2013)	Age- and language-matched children with autism (n=27), autism spectrum disorder (n=14), and developmental disorders without autism (n=16).	Autism Diagnostic Observation Schedule-General and previous clinical diagnoses.	Test of Pretend Play (ToPP), with an additional rating of 'playful pretense'.	<ul style="list-style-type: none"> <li>» Children with autism showed less playful pretend than participants with developmental disorders who did not have autism.</li> <li>» Limitations in creative, playful pretend among children with autism relate to their restricted interpersonal communication and engagement.</li> </ul>

### 1.2.5 Substance use/abuse

Beveridge et al. argued that while the medical establishment generally takes a negative view on alcohol use and especially abuse, the opposite is true for the lay public and many writers and artists (1999). They prize alcohol for its ability to make new creative insights, and courageous drinking has long been associated with artistic personality. Rather than being a sign of personal failing, alcoholism is taken as evidence of artistic integrity. The studies investigating this question have generally approached the question in two ways. One is to investigate the direct effect on the creative process under intoxication; the other is to study the effects on creative productivity in the long run under excessive drinking and drug abuse.

#### 1.2.5.1 Alcohol use/abuse

Brunke et al. gave 11 male social drinkers a creative writing task under alcohol (1.1 ml ethanol/kg body weight) and placebo condition (1992). All individuals participated in both conditions, and results

demonstrated an increase of total novel tropes, as well as the quota of novel tropes compared to total novel tropes in the alcohol condition. In addition, subjects wrote more words when intoxicated. Jarosz et al. similarly showed that individuals intoxicated with alcohol (.88 g ~1.10 ml/kg body weight) solved more problems on the Remote Associate Test than their sober counterparts (2012). Lowe expanded these findings in a study of 16 social drinkers performing under alcohol (0.83 ml/kg body weight) and placebo condition (1994). The creative performance of subjects scoring low on creativity in the placebo condition was enhanced by alcohol, whereas those scoring high in creativity during the placebo condition were conversely compromised in creative performance by alcohol. Further, Lang et al. used a comparably lower dose of alcohol (0.6 g ~0.75 ml/kg body weight) with minimal effects on creativity. However, those individuals who thought they had received alcohol gave more positive evaluations of their creative abilities than did subjects who thought they were in the non-alcohol group (1984). Similar results were presented by Lapp et al. in subjects receiving lower doses of alcohol (max 0.4 ml/kg body weight) (1994).

While studies on alcohol intoxication suggest positive benefits on the creative process, studies on excessive alcohol intake in the long run provide more mixed results. Ludwig's study on 1005 outstanding individuals who had their biographies published in the New York Times Book Review from 1960 to 1990 found a general increase in alcohol abuse in artists (1992, 1995). Similar results were suggested by Post in his study of 291 world famous men and 100 well-known prose and play writers (1994, 1996). Again, writers seem to stand out from other artists, further suggested by the results of the study by Andreasen on writers in the Iowa Writer's Workshop (1987). Thirty percent of the writers had alcohol abuse compared to 7 percent of the controls. On the other hand, when Ludwig investigated the writers in his previous cohort specifically, alcohol use proved detrimental to productivity in over 75 percent of the sample, especially in the latter phases of their drinking careers (1990). Alcoholic fathers compared to non-alcoholic fathers performed significantly lower on divergent thinking tests in a study by Noble et al. (1993). Similar results were suggested in the sons of these fathers. Plucker et al. could not validate these findings in a larger group, but instead found no appreciable effect on students' creative achievement related to parental alcohol and drug problems (1998).

#### 1.2.5.2 *Drug use/abuse*

One study tested the influence of cannabis on creativity (Schafer et al., 2012). Cannabis users were tested on a day when sober and another day when intoxicated with cannabis. Results revealed that cannabis increased verbal fluency in individuals with low creativity

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in non-intoxicated phase to the same level as that of individuals with high creativity. No effect on creativity was seen on those individuals scoring high on creativity in non-intoxicated phase. Ludwig's study on 1 005 prominent individuals suggested increased drug abuse in those active within creative arts (1992, 1995).

TABLE 3. SUMMARY OF STUDIES PRIMARILY INVESTIGATING SUBSTANCE USE/ABUSE DISORDERS

REFERENCE	STUDY SAMPLE	ASSESSMENT OF MENTAL DISORDER	DEFINITION OF CREATIVITY	FINDINGS
(Lang et al., 1984)	40 male undergraduate social drinkers were assigned to one of four treatments in a balanced placebo design. Those actually receiving alcohol consumed a mixture containing .6 g ~0.75 ml of ethanol per kg of body weight.	Pretest instrument, including Multiple Affect Adjective Check List, was administered containing questions about demographic characteristics, routine drinking behavior, and beliefs about own creativity and alcohol's effects on it.	Figural portion and the Unusual Uses subtest of the Verbal portion of the Torrance Tests of Creative Thinking.	<ul style="list-style-type: none"> <li>» Minimal effects of beverage manipulations on measured.</li> <li>» Individuals who thought they had received alcohol gave significantly more positive evaluations of their creative.</li> </ul>
(A. M. Ludwig, 1990)	Biographies of 34 well known, heavy drinking, 20th century writers, artists, composers, and performers.	For the entire pool of subjects, the same type of information was systematically gathered from at least one major, published biography and transposed onto elaborate data collection forms.	Their biographies had received a review in the New York Times Book Review from 1965 to 1990.	<ul style="list-style-type: none"> <li>» Alcohol use proved detrimental to productivity in over 75% of the sample, especially in the latter phases of their drinking careers.</li> <li>» It appeared to provide direct benefit for about 9% of the sample, indirect benefit for 50%.</li> </ul>
(Brunke & Gilbert, 1992)	11 male social drinkers participated in a creative writing task under two conditions, alcohol and placebo. Alcohol condition was a high dose with 1.1 ml ethanol/kg bodyweight.	Subjects were tested individually and were randomly assigned to one of the two beverage sequences: alcohol on Day 1 and placebo on Day 2, or placebo on Day 1 and alcohol on Day 2.	Figurative language was scored using a procedure adapted from a manual developed by Barlow, Kerlin, and Pollio (1970) for use in researching metaphor usage.	<ul style="list-style-type: none"> <li>» Subjects wrote more novel tropes while intoxicated than when sober.</li> <li>» Alcohol condition produced a higher proportion of novel tropes to total tropes.</li> <li>» Subjects wrote more words when intoxicated.</li> </ul>

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(Noble et al., 1993)	A battery of creativity tests was administered to 56 families (fathers, mothers, and their pubescent sons) representing three groups. Group A+ was comprised of recovering alcoholic fathers with a family history of alcoholism (n=19). Group NA+ consisted of nonalcoholic fathers with a family history of alcoholism (n=18). Group NA- was composed of nonalcoholic fathers without a family history of alcoholism (n=19).	Diagnosis of fathers' alcoholism was made according to DSM-III-R criteria. None of the mothers or sons in the three family groups were alcoholic.	Creativity Personality Scale, the four Origenice/Intellectence scales from the Adjective Check List, and the How Do You Think Test. Moreover, fathers and sons received two divergent thinking tests, and mothers rated their sons using a special scale from the Adjective Check List. The Wechsler Adult Intelligence Scale was administered to the fathers and the Wechsler Intelligence Scale for Children-Revised was given to the sons.	<ul style="list-style-type: none"> <li>» Sons of alcoholics scored significantly lower than the other two groups of boys on the Creative Personality Scale.</li> <li>» Alcoholic fathers and their sons scored higher than the other two groups on the High Origenice/Low Intellectence scale (AI).</li> <li>» Sons of alcoholic fathers showed significantly lower scores than the other two groups of boys on the How do you think.</li> <li>» On the two divergent thinking tests, alcoholic fathers performed significantly lower than the two groups of nonalcoholic fathers. Sons of alcoholic fathers showed a similar trend, though it was not significant.</li> </ul>
(Lapp et al., 1994)	116 men.	0.0, 1.1, or 2.2 ml 80% vodka ► 0.0, 0.02, or 0.04 ml alcohol/dl blood.	A card-sorting task assessing creative synthesis of emergent relations.	<ul style="list-style-type: none"> <li>» No pharmacological effect of alcohol on the creative combinations that subjects produced.</li> <li>» Novelty and structural recombination were enhanced when subjects thought they had consumed alcohol.</li> </ul>
(Lowe, 1994)	16 social drinkers (8 females, 8 males) performed under 2 conditions, alcohol and a placebo.	Alcohol dose =0.83 ml ethanol/kg body weight.	Verbal forms of the Torrance Creativity Test.	<ul style="list-style-type: none"> <li>» Significant group differences in the alcohol-creativity interaction were noted; performance of higher-scoring in the placebo condition; subjects was impaired (mean: 241.9 ►202.7) by alcohol whereas that of lower-scoring subjects was enhanced (mean: 147.1►179.2).</li> </ul>
(Plucker & Dana, 1998)	The impact of parental substance abuse problems on 163 undergraduates' creative achievement.	Core Alcohol and Drug Survey. Students also reported whether their parents had substance abuse problems.	Creative Behavior Inventory.	<ul style="list-style-type: none"> <li>» Parental alcohol and drug problems did not have an effect on students' creative achievement.</li> </ul>

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(Schafer et al., 2012)	160 cannabis users were tested on a day when sober and another day when intoxicated with cannabis. Quartile splits compared those lowest (n=47) and highest (n=43) in Creative Achievement Questionnaire (CAQ).	A sample of cannabis was taken to be analyzed for levels of THC. Psychotomimetic States Inventory (PSI), Schizotypal Personality Questionnaire (SPQ), Weschler Test of Adult Reading (WTAR), Spielberger Trait Anxiety Inventory (STAI), Severity of Dependence Scale (SDS), Beck Depression Inventory (BDI).	Verbal fluency task, category fluency task, Remote Associates Test (RAT), CAQ.	<ul style="list-style-type: none"> <li>» Cannabis increased verbal fluency in low creatives to the same level as that of high creatives.</li> <li>» The high creativity group was significantly higher in trait schizotypy, but this was not linked to the verbal fluency change.</li> </ul>
(Jarosz et al., 2012)	40 male social drinkers (20 in the alcohol (A) intoxication condition and 20 in the sober comparison condition).	Operation Span Task (OSpan), alcohol condition (.88 g ~1.10 ml/kg body weight).	Remote Associates Test (RAT).	<ul style="list-style-type: none"> <li>» A solved more RAT problems than their sober counterparts.</li> <li>» This increase in solution success was accompanied by a decrease in time to correct solution for A.</li> <li>» A rated their experience of problem solving as being more insightful.</li> </ul>

### 1.2.6 Neurological disorders

Five studies investigated the effects of neurological disease on creativity. The results of these studies are suggested to aid further understanding of the neurocognitive processes underlying creativity.

#### 1.2.6.1 *Dementias, Parkinson's disease and other neurological disorders*

Miller et al. interviewed 69 patients with frontotemporal dementia (FTD) regarding their visual abilities (1998). Five of the patients turned to artistic activities in their early disease. These all had the temporal variant of FTD, and the authors suggested that loss of function in the anterior temporal lobes may lead to 'facilitation' of artistic skills. Souza et al. later demonstrated that individuals with frontotemporal lobar degeneration with severe *frontal* degeneration (fvFTLD) were strongly impaired in all dimensions of the Torrance Test of Creative Thinking (2010). The authors proposed that any appearance of artistic talent in patients with fvFTLD is explained by the release of unintentional behaviors, rather than by the improvement of creative thinking. These results were generally supported by Abraham et al., however, in contrast they also showed that individuals with lesions in the basal ganglia and frontopolar areas demonstrated *better* performance in presence of semantic constraints when producing creative responses (2012). Drago et al. reported on a single visual artist with Lewy body dementia (LBD),

where representational ratings for the pictures painted with LBD were lower than the picture painted before development of LBD (2006). All the artistic qualities measures temporally declined except *novelty*. Souza et al. also included patients with Parkinson’s disease (PD), but these demonstrated no differences with regards to the Torrance Test of Creative Thinking compared to controls (2010). Canesi et al. argued that any increased artistic-like production in patients with PD is not associated with impulsivity or impulsive control disorders, but rather represent innate skills in a subset of predisposed patients with PD released by dopaminergic therapy (2012).

TABLE 4. SUMMARY OF STUDIES PRIMARILY INVESTIGATING NEUROLOGICAL DISORDERS

REFERENCE	STUDY SAMPLE	ASSESSMENT OF MENTAL DISORDER	DEFINITION OF CREATIVITY	FINDINGS
(B. L. Miller et al., 1998)	69 patients with frontotemporal dementia (FTD). 5 became artists in the early stages of FTD.	Mini-Mental State Examination, Wisconsin Card Sorting, Stroop tasks, modified Rey-Osterrieth Complex Figure Copy, MRI, SPECT, autopsy,	Interview.	» 4 of the 5 patients, who became artists, had the temporal variant of FTD.
(Drago et al., 2006)	A visual artist with Lewy body dementia (LBD).	-	<i>Study 1</i> evaluated two paintings of the same subject matter, one painted before the illness and the other after the onset. <i>Study 2</i> evaluated a collection of his paintings from the time before illness until the time of ceased painting when he was suffering.	» Study 1 found representational ratings for the picture painted with LBD was lower than the picture painted before development of LBD. » Study 2 found that all the artistic qualities measures temporally declined except novelty.



## INTRODUCTION

<p>(de Souza et al., 2010)</p>	<p>17 patients with frontotemporal lobar degeneration (fvFTLD), 12 nondemented Parkinson's disease (PD) patients, and 17 healthy controls.</p>	<p>Revised Lund–Manchester consensus criteria, MRI in all patients, and 13 out of 17 patients had a SPECT, MMSE, Frontal Assessment Battery (FAB), Clinical Dementia Rating (CDR), MADRS, Trail Making Test (TMT), Stroop test, modified Wisconsin Card Sorting Test, verbal fluency, Working memory was evaluated with direct and indirect visual and verbal spans, Social and Emotional Assessment (SEA).</p>	<p>Torrance Test of Creative Thinking (TTCT).</p>	<ul style="list-style-type: none"> <li>» FvFTLD were strongly impaired in all dimensions of the TTCT, compared to PD and controls.</li> <li>» Disinhibited and perseverative responses were observed only in fvFTLD patients.</li> <li>» Poor creativity was positively correlated with several frontal tests.</li> <li>» Poor creativity was also correlated with prefrontal hypoperfusion.</li> </ul>
<p>(Canesi et al., 2012)</p>	<p>36 Parkinson's disease patients with (PD-c) or without (PD-nc) increased artistic-like production and 36 healthy controls (HC).</p>	<p>Diagnosis of PD according to UK Brain Bank criteria. Mini-mental state examination, frontal lobe assessment battery, clock drawing test, Rey figure copy and recall, verbal and phonemic fluency, and Raven matrices. Unified Parkinsons Disease Rating Scale motor score (UPDRS-III) and Hoehn-Yahr staging.</p>	<p>Artistic-like productivity was defined to be enhanced if patients reported working on any form of art more than 2 h per day after the introduction of dopaminergic treatment. Torrance Test of Creative Thinking (TTCT), Barratt Impulsiveness Scale (BIS-11A), the Minnesota Impulsive Disorders Interview (MIDI), and the Punding Rating Scale.</p>	<ul style="list-style-type: none"> <li>» Mean TTCT score of PD-c was found to be similar to HC, and both PD-c and HC had significantly higher TTCT scores than patients with PD-nc.</li> <li>» No correlation was found between TTCT, BIS-11A, and MIDI.</li> </ul>
<p>(Abraham et al., 2012)</p>	<p>74 patients recruited from the Neurological Day Clinic database. Healthy control participants were selected to match each patient.</p>	<p>Patients were examined by the clinic's chief neurologist prior to the study. Lesion sites were determined by MRI and evaluated by an experienced neuroanatomist. Patients had lesions mainly in the frontal lobe (FL; 9 females, 20 males, parietal–temporal lobe (PTL; 1 females, 10 males), or basal ganglia (BG; 4 females, 12 males).</p>	<p>Conceptual expansion task, the creative imagery task, the constraints of examples task, the alternate uses task, Remote Associates Test (RAT), and analytical problem solving tasks (insight and incremental).</p>	<ul style="list-style-type: none"> <li>» PTL and frontolateral groups revealed poorer overall performance with PTL demonstrating problems with fluency measures, whereas the frontolateral were also less proficient at originality.</li> <li>» BG and frontopolar groups demonstrated superior performance in the ability to overcome constraints imposed by salient semantic distractors when generating creative responses.</li> </ul>

### 1.2.7 Other mental disorders

Some studies and mental illnesses do not fall into any of the categories reviewed above. For example, studies investigating prominent individuals (i.e., big-C) have often reported increased occurrence of other mental disorders, such as in Ludwig's study of 1 005 eminent individuals (1992, 1995). Those active within the creative arts were suggested to have an increased occurrence of anxiety disorders. Post also argued for unusual personality characteristics in his study of 291 world famous men (1994). Glover et al. investigated students aged 14–19 years without ( $n=200$ ) and with ( $n=194$ ) behavioral problems, and showed that those having behavioral problems scored significantly higher on flexibility and originality, than did students with no behavioral problems (1976). Akinola et al. demonstrated that social rejection was associated with greater artistic creativity, and that this was especially evident among those lower in dehydroepiandrosterone (DHEAS). The later was mediated through an increase in negative emotions, implicating DHEAS as an indicator of affective vulnerability (2008). However, Smith et al. argued that anxiety did not facilitate creativity in *patients* with anxiety disorders, the opposite being the case for controls (1983). They concluded that the main hindrance to creative functioning is low tolerance of the anxiety accompanying creative efforts.

Suicide and suicide ideation has also been investigated in relation to creativity. Mraz et al. demonstrated that problem generation scores were significantly correlated (*fluency* positively, *flexibility* negatively) with suicide ideation (1994). Preti et al. investigated suicide in a sample of 4 564 eminent artists who died in the 19th and 20th centuries (2001). Musicians as a group had lower suicide rates than literary and visual artists. Stack used official suicide statistics and demonstrated that artists had a 125 percent higher risk of suicide than among non-artists (1996).

One study specifically investigating a genetic hypothesis for the association of creativity and mental illness was performed by McNeil (1971). In this study, 43 adults adopted by non-biologically related families were compared to 23 non-creative adoptees. Mental illness rates in the adoptees were positively related to their creative abilities, mental illness rates of the biological parents were positively related to the creative abilities of the adoptees, but mental illness rates among adoptive parents were independent of the adoptees' creative abilities.

Study I and II of this thesis investigates the association of creativity and psychopathology by examining the occurrence of creative occupations in patients with a wide array of different psychiatric disorders and their healthy relatives in comparison to controls.

INTRODUCTION

TABLE 5. SUMMARY OF STUDIES INVESTIGATING OTHER MENTAL DISORDERS

REFERENCE	STUDY SAMPLE	ASSESSMENT OF MENTAL DISORDER	DEFINITION OF CREATIVITY	FINDINGS
(McNeil, 1971)	43 adults adopted by non-biologically related families were compared to 23 non-creative adoptees. The final population consisted of 50 adoptees.	Rates of mental illness were determined among all included subjects and their parents and siblings.	Creative ability was operationally defined by a committee evaluation. The subjects were divided into three groups; high-, above-average-, and low-creative ability.	<ul style="list-style-type: none"> <li>» Mental illness rates in the adoptees were positively related to their creative abilities.</li> <li>» Mental illness rates of the biological parents were positively related to the creative abilities of the adoptees.</li> <li>» Mental illness rates among adoptive parents were independent of the adoptees' creative abilities.</li> </ul>
(Glover & Tramel, 1976)	Students 14-19 yrs without (n=200) and with (n=194) behavioral problems.	Students with behavioral problems had been suspended from school on at least one occasion during the current school year.	Unusual Uses subtest of the Torrance Tests of Creative Thinking, Verbal Form b.	» Students identified as having behavioral problems scored significantly higher on two components of creative ability, flexibility and originality.
(Paget, 1979)	16 emotionally disturbed preschoolers ranging in age from 3 to 6 years.	Data on file for the children were gathered concerning their intelligence, socio-emotional development, and length of time in treatment.	Torrance preschool measure.	» Results suggest that the emotionally disturbed preschoolers were as creative as normal preschoolers.
(Smith & Carlsson, 1983)	31 psychiatric patients with anxiety and 43 controls.	Interview	Interview	» Anxiety did not facilitate creativity in patients as was the case with controls.
(Mraz & Runco, 1994)	81 college students.	Scale for Suicide Ideation (BSSI), Suicide Ideation Scale (SSI), Hopelessness Scale (HS), Suicide Opinion Questionnaire (SOQ), Perceived Stress Scale (PSS), Student Stress Inventory.	Divergent thinking tasks.	» Problem generation scores were significantly correlated (fluency positively, flexibility negatively) with suicide ideation.
(Stack, 1996)	Artists aged 21-64 years (n=?).	Official suicide statistics.	Artists were defined as authors, musicians, actors, painters, and dancers.	» After controlling for gender and sociodemographic variables, Artists had a 125% higher risk of suicide than among non-artists

CREATIVITY AND PSYCHOPATHOLOGY

(Preti & Miotto, 1999)	Artists found in Garzanti's Encyclopaedia (n=3093).	Suicide, based on all the biographies cited in the two repositories for eminent people eligible for the study.	1300 writers, 692 poets, 267 dramaturgians and comedians, 210 architects, 531 painters, 93 sculptors.	<ul style="list-style-type: none"> <li>» Comparison by profession indicates that poets and writers exceed the mean suicide ratio of the sample.</li> <li>» Painters and architects, conversely, have a clearly lower risk than the mean.</li> </ul>
(Preti et al., 2001)	The percentage of deaths by suicide in a sample of 4564 eminent artists who died in the 19th and 20th centuries. Of the sample, 2259 were writers, 834 visual artists, and 1471 musicians.	Suicide.	Eminence was defined as a record in Garzanti's Art, Literature, and Music Encyclopaeda.	<ul style="list-style-type: none"> <li>» 63 suicides in the sample (1.3% of total deaths).</li> <li>» Musicians (0.2%) as a group had lower suicide rates than literary (2.3%) and visual artists (0.7%).</li> </ul>
(Chavez-Eakle, Lara, & Cruz-Fuentes, 2006)	30 with high creative achievement (HC) dedicated to full-time scientific or artistic creation, 30 controls administrative staff and graduate students, 30 psychiatric outpatients.	Temperament and Character Inventory (TCI), Symptom Check List (SCL)-90. Three different psychiatrists confirmed psychiatric diagnosis. Included diagnoses were mainly major depressive disorder and anxiety disorders.	Torrance Tests of Creative Thinking.	<ul style="list-style-type: none"> <li>» HC scored low on psychopathology.</li> <li>» There were strong negative correlations between creativity and psychopathology on all subscales.</li> </ul>
(Akinola & Mendes, 2008)	96 young adults (65 females, 31 males).	Saliva sample that assayed for dehydroepiandrosterone (DHEAS), experiment of social approval or social rejection, Positive and Negative Affect Schedule.	Abbreviated Torrance Test for Adults, an artistic creativity task (CAT).	<ul style="list-style-type: none"> <li>» Social rejection was associated with greater artistic creativity; however, the interaction between affective vulnerability</li> <li>» (lower baseline DHEAS) and condition was significant, suggesting that situational triggers of negative affect were especially influential among those lower in DHEAS, which resulted in the most creative products.</li> </ul>
(Silvia & Kimbrel, 2010)	189 university students (150 females, 39 males).	Depression and Anxiety subscales of the Depression Anxiety Stress Scales, Social Interaction Anxiety Scale.	3 divergent thinking tasks, 9-item Creativity Scale for Different Domains, Creative Behavior Inventory, Creative Achievement Questionnaire.	<ul style="list-style-type: none"> <li>» Overall, measures of anxiety, depression, and social anxiety predicted little variance in creativity. Few models explained more than 3% of the variance.</li> </ul>

### 1.3 LEADERSHIP AND BIPOLAR DISORDER

Related to the question of creativity and psychopathology is the historical notion that bipolar disorder (*melancholia*) is associated with a predisposition for great leadership in general and political inclination in particular - evident in Aristotle's famous quote referenced in the introduction of this thesis (Aristotle & Barnes, 1984).

This idea gathers some support in retrospective studies showing that more than 40% of world famous politicians have suffered from episodes of depression (Post, 1994), and that famous politicians and business persons are more disposed to depressive and manic episodes than the general population (Arnold M. Ludwig, 1995).

More recently, Ghaemi has suggested that diametrically different leadership personalities are essential when times are calm and prosperous compared to times of change and crisis (2011). In times of stability, less stress is placed on the leader and aspects such as detail-orientation and deliberate decision-making with clearly defined roles are important, while in times of change, openness, creativity, and enthusiasm are essential to succeed as a leader. Personality traits associated with bipolar disorder would hence be coupled to the type of transformational leadership essential in changeable times. Ghaemi argues that many historical leaders, e.g., Winston Churchill, Abraham Lincoln, and Napoleon Bonaparte, active in times of change, displayed features of fulminant bipolar disorder or tendencies towards the bipolar spectrum (Ghaemi, 2011).

Study IV of this thesis investigates the idea of an association between leadership traits and bipolar disorder by considering data from the mandatory military service on leadership potential as well as through analyzing data on executive professions, and political occupations, specifically.

### 1.4 GENETICS OF CREATIVITY

Some of the most exciting findings in modern creativity research is related to biological correlates of originality, novelty, and insight (Runco, 2007). Recent technical advances in, e.g., molecular genetics now provide possibilities for targeting the genetic underpinnings of creativity (James C. Kaufman & Sternberg, 2010; Runco, 2007).

The study of familiarity in creativity related traits has a long history with hallmark studies such as Galton's *Hereditary Genius: an enquiry into its laws and consequences* (1869). Barron early demonstrated a small but significant heritability (genetic component) for creative thinking and ideational fluency (1970). However, many studies of heritability in creativity use small samples and estimates therefore vary considerable between studies. One of the aims of this thesis is therefore to provide the currently best estimate for the heritability of creativity (study V).

There have also been suggestions for a genetic mediation of the link between creativity and mental illness. For example, in Karlsson's investigations of relatives to patients with schizophrenia, he concluded that certain branches of kindreds were high in both schizophrenia and giftedness, whereas others were low in both (1970). In study I, we approached this question by specifically investigating half-siblings of patients with schizophrenia and bipolar disorder. An attempt to differentiate between the genetic and environmental impact on the accumulation of creativity and psychopathology was also conducted in the previously reviewed adoption study by McNeil (McNeil, 1971). The results of this study were interpreted as evidence for the influence of pre-birth (e.g., genes, intrauterine) factors on the relationship between creative ability and mental illness. We provide a thorough review of studies related to the genetics of creativity in study V.

### 1.5 AN EVOLUTIONARY FRAMEWORK FOR CREATIVITY AND PSYCHOPATHOLOGY

Central to the study of creativity and psychopathology is if this association may explain the paradox of severe psychiatric disorder in light of high heritability (genetic component) and decreased fertility. This *evolutionary paradox* was early noted by the Swedish psychiatrist Essen-Möller in patients with schizophrenia (1959). Later research has validated these findings in most severe psychiatric disorders (Uher, 2009).

Biological evolution is in strict terms defined as *descent with modification* (Futuyma, 2009). Thus, essential for evolution is *variation* and *selection*. In that certain traits are inherited, there is a variation in their representation, and a selection of these traits; some traits will increase, whereas others will decrease. The definition includes both large scale (origin of species) and small scale (changes in gene frequency in a given population) evolution.

The mechanisms underlying biological evolution are diverse. Given that genes predispose to specific traits, mutation, migration and sexual reproduction will increase variation in these traits. Conversely, natural selection (including sexual selection) will result in some traits (and therefore genes) to be preserved and increased in frequency relative to other traits. Genes (and therefore traits) may also in a purely random effect increase or decrease in frequency, which is called genetic drift, which is of distinctive importance in small populations.

However, only natural selection (including sexual selection) leads to adaptation, since the selection rewards traits that result in increased function. Function should be seen in a larger context and to humans from a reproductive perspective, i.e., fitness, since it is through reproduction that sexual organisms can spread their genes and thus traits.

## INTRODUCTION

Except for the notion that psychiatric disorders did not constitute an evolutionary disadvantage in earlier human history (*ancestral neutrality*), there are two major evolutionary hypotheses why severe psychiatric disorders and underlying genes have prevailed in spite of heavy selection against them (Uher, 2009).

The first, *balancing selection* hypothesis, assumes that alleles (gene variants) associated with psychiatric disorder in patients and their relatives also hold adaptive advantages that increase fitness (Huxley, Mayr, Osmond, & Hoffer, 1964). This hypothesis is congruent with studies demonstrating a peak of creativity in relatives of patients with psychiatric disorder, rather than in the patients themselves (Richards et al., 1988). Thus, when not succumbing to illness, the relatives of patients can benefit from increased creativity, which consequently could increase their fitness.

The alternative *mutation-selection* hypothesis suggests that psychiatric disorders reflect mutational load upheld by constantly recurring mutations (Haldane, 1927). This theory explains the prevailing prevalence of severe psychiatric disorders despite reductions in fertility, without assuming any compensatory evolutionary advantage, such as creativity.

In study III, we addressed the evolutionary framework by investigating the fecundity of individuals with different psychiatric disorders and their healthy siblings on a total population scale. We aimed to validate if there truly is a selection against traits related to different psychiatric disorders, and to investigate if this is compensated for in healthy siblings of patients. If the latter is true, this would point towards the balancing selection hypothesis.

## 2 Aims



## AIMS

THE PRIMARY AIM of this thesis is to explore the putative association between creativity and psychopathology using large scale population based epidemiological methods. The secondary aim is to elucidate if such an association may be mediated through genetic factors under positive selection. More specifically our goals were:

**Study I:** to conduct a population based study of the occurrence of creative occupations among individuals with schizophrenia, bipolar disorder, or unipolar depression and their relatives compared with controls without these disorders and their relatives.

**Study II:** to extend the findings in study I by estimating the occurrence of creative occupations in patients with schizoaffective disorder, anxiety disorders, alcohol abuse, drug abuse, autism, ADHD, anorexia nervosa, and completed suicide, and their first-, second-, and third-degree relatives in comparison to non-diagnosed controls.

**Study III:** to examine the reproductive fitness (fertility) of patients with psychiatric disorders in comparison with their unaffected siblings and to evaluate the level of selection on causal genetic variants.

**Study IV:** to investigate leadership traits in persons with bipolar disorder with and without psychiatric comorbidity, and their healthy siblings, compared to matched controls, and secondly to investigate if these patients and their siblings have an increased likelihood for holding executive professions in general, and political professions in particular.

**Study V:** to systematically review studies on the heritability in creativity, and to carry out both the first total population estimate of heritability in creative professions, as well as an analysis of heritability in a large twin cohort surveyed with the CAQ.

### **3 Materials and methods**

### 3.1 DATA SOURCES

#### 3.1.1 Register data

##### 3.1.1.1 *National Patient Register*

The National Patient Register (NPR, National Board of Health and Welfare) provided discharge diagnoses for all inpatient treatment episodes in Sweden 1973-2009, and restricted coverage of outpatient specialist physician (other than general practitioners) treatment episodes in 2001-2009. Diagnoses were coded according to the 8th, 9th, and 10th editions of the ICD (1969-1986, 1987-1996, 1997-).

The use of registers in psychiatric research is well established (Byrne, Regan, & Howard, 2005). The general validity of both somatic and psychiatric diagnoses in the NPR was recently reviewed with an estimated positive predictive value of 85-95 % (Ludvigsson et al., 2011).

##### 3.1.1.2 *Cause of Death Register*

The Cause of Death Register (CDR, National Board of Health and Welfare) provided data on completed suicides in Sweden 1952-2009. The register contains information on all deaths among Swedish residents including date and causes according to ICD.

##### 3.1.1.3 *The Multi-Generation Register*

The Multi-Generation Register (MGR, Statistics Sweden) permitted identification of biological relatives of an index person, including all individuals born in Sweden since 1932 and registered as living in Sweden after 1960. Biological fathers are assumed to be the husbands of the mothers at the time of birth or those identified 'by acknowledgment' for unwed mothers.

##### 3.1.1.4 *Swedish Twin Registry*

The nationwide population based Swedish Twin Registry (STR, Karolinska Institutet) includes essentially all twins born in Sweden since 1886. It is one of the world's largest twin databases. Zygosity was determined either by questions about intra-pair physical similarities in childhood, genotyping, or by being of opposite sex (Magnusson et al., 2013).

##### 3.1.1.5 *National censuses*

National censuses based on compulsory self-report questionnaires completed by all adult citizens in 1960, 1970, 1975, 1980, 1985 and 1990 provided information on occupations in the entire Swedish population. The censuses are more than 99% complete (Norman et al., 2002).

3.1.1.6 *Longitudinal Integration Database for Health Insurance and Labor Market Studies*

The Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA, Statistics Sweden) incorporates annual total statistics from the public sector, and selected from 10,000 companies in the private sector including all, but not restricted to, companies with more than 500 employees (Statistiska centralbyrån [Statistics Sweden], 2011). The database was used in conjunction with the national censuses to acquire data on occupations.

3.1.1.7 *Military Service Conscription Register*

The Military Service Conscription Register (Swedish Defense Recruitment Agency) provided IQ test results for essentially all 18-19 year-old men conscripted between 1970 and 2009, as well as data from a semi-structured interview of leadership potential, i.e., *officer suitability*. The assessment of officer suitability was restricted to those with IQ test results of the conscript population mean or higher.

3.1.1.8 *Total Population Register*

The Total Population Register (Swedish Tax Agency) provided some descriptive data, e.g., income, marital status, and place of residence.

3.1.2 **Screening Across the Life-span Twin Younger cohort**

The Screening Across the Life-span Twin Younger (SALTY) cohort study was conducted 2009-2010. A survey was mailed to 24 916 Swedish twins born between 1943 and 1958 (Magnusson et al., 2013). A total of 11 372 respondents (46%) consented to have their answers stored and analyzed. Participants were also offered to take part in a web survey, which included the CAQ.

3.2 **MEASURES**

3.2.1 **Psychopathology**

The reader is referred to standard textbooks in psychiatry for an overview of the different psychiatric disorders investigated in this thesis (Herlofson et al., 2009). There are currently two diagnostic systems applied for the nosology of psychiatric disorders: 1) the International Classification of Diseases (*ICD*) published by the World Health Organization and used for worldwide statistics as well as for reimbursement systems, and 2) the Diagnostic and Statistical Manual of Mental Disorders (*DSM*) published by the American Psychiatric Association. The ICD is currently in its tenth version (*ICD-10*) (2004), while the DSM was recently released in its fifth version (*DSM-5*) (American Psychiatric Association & American Psychiatric Association. *DSM-5 Task Force*.,

2013). ICD-10 contains prototypical descriptions of different mental disorders, while the DSM-5 have a criteria based approach. The latter was established in the 1980s with DSM-III by the American Psychiatric Association, and headed by the chair of the DSM task force Robert Spitzer. This system has dominated psychiatric research and clinical diagnostics the last decades, although Sweden and many other countries formally applies the ICD-10 in health care. The DSM therefore contains a translation to ICD. While the criteria based diagnostics has received much support for enabling research, it has also received criticism on the grounds of overly simplifying psychiatric phenomenology with one result being an inflation of psychiatric disorders (N. C. Andreasen, 2007; Frances, 2013).

Below is a brief summary of the psychiatric disorders investigated in this thesis based on DSM-5 definitions.

### 3.2.1.1 *Psychosis*

Psychosis in its contemporary meaning implies impaired reality-testing ability (Stern & Massachusetts General Hospital., 2008). The most important features are hallucinations and delusions. Psychosis is not a mental disorder, but a symptom present across different psychiatric disorders.

The term was established in 1845 by Feuchtersleben for all mental disorders since he believed that these were ‘diseases of the personality’ resulting from an interplay between body and mind (Beer, 1996). The purpose was to refrain from using other than present descriptions of mental disorders, such as ‘Geisteskrankheiten’ and ‘Seelenstörungen’ placing too much emphasis on the mind. The initial meaning of psychosis was thus simply *mental disorder*. This definition was upheld by Kraepelin in the first edition of his textbook published in 1896, but successively narrowed and finally in the ninth edition, Kraepelin designated *dementia praecox* (renamed schizophrenia by Eugen Bleuler) and *manic-depressive insanity* as the only two true psychotic disorders. This idea continues in today’s nosological division between schizophrenia and bipolar disorder (American Psychiatric Association & American Psychiatric Association. DSM-5 Task Force., 2013), although the interpretation of psychosis has now changed into being a symptom of compromised reality-testing. Still, psychosis in this contemporary meaning is also a defining clinical feature of schizophrenia and often present in severe bipolar disorder.

### 3.2.1.2 *Schizophrenia*

DSM-5 defines schizophrenia as involving a range of cognitive, behavioral, and emotional dysfunctions. Formally, at least two of the following symptoms has to be present for at least one month: delusions,

hallucinations, disorganized speech (e.g., frequent derailment or incoherence), grossly disorganized or catatonic behavior, or negative symptoms (i.e., diminished emotional expression or avolition). Continuous signs of disturbance have to be present for at least six months.

The lifetime prevalence of schizophrenia is approximately 0.3%–0.7%, with psychotic symptoms generally emerging between the late teens and the mid-30s.

3.2.1.3 *Schizoaffective disorder*

A diagnosis of schizoaffective disorder requires that a major depressive or manic episode (see below) arise concomitantly with symptoms of schizophrenia and that the mood symptoms are present for a majority of the total duration of the active schizophrenic periods. However, delusions or hallucinations also have to be present for two or more weeks without a concurrent major depressive or manic episode.

3.2.1.4 *Bipolar disorder*

The diagnosis of bipolar disorder requires a manic (bipolar I disorder) or a hypomanic (bipolar II disorder) episode. A *manic* episode is defined as a period of continuously elevated, expansive, or irritable mood and increased goal-directed activity or energy, lasting at least one week (or any duration if hospitalization is necessary), and leading to marked impairment in functioning. A *hypomanic* episode is defined as lasting for at least four days, without necessarily leading to marked impairment in functioning. The majority of individuals meeting the criteria for a hypomanic/manic episode will also experience a *major depressive episode* (see major depressive disorder below) in their lives.

The 12-month prevalence estimate in the United States was 0.6% for bipolar I disorder and 0.8% for bipolar II disorder as defined in DSM-IV. Mean age at onset of the first manic, hypomanic, or major depressive episode is approximately 18 years for bipolar I disorder, and slightly later for bipolar II disorder.

3.2.1.5 *Unipolar depression (major depressive disorder)*

Major depressive disorder requires a two week period or more of at least one of the two symptoms: depressed mood or loss of interest or pleasure, together with other associated symptoms. The symptoms must cause clinically significant distress or impaired function.

Twelve-month prevalence of major depressive disorder in the United States is approximately 7%. It may debut at any age, but the likelihood of onset increases considerably with puberty.

3.2.1.6 *Anxiety disorders*

Anxiety disorders include disorders that share symptoms of

unwarranted fear and anxiety, such as panic disorder and social phobia. These are common disorders with prevalence rates ranging from approximately 2-3% for panic disorder to 7% for social phobia.

3.2.1.7 *Alcohol and drug abuse (substance use disorders)*

The diagnosis of a substance use disorders is based on a pathological pattern of behaviors related to use of the substance. In the United States, the twelve-month prevalence of alcohol use disorder among adults is estimated to be 8.5%.

3.2.1.8 *Autism spectrum disorder*

The main features of autism spectrum disorder are continuous impairment in social communication and interaction, and restricted, repetitive patterns of behavior, interests, or activities. These symptoms debut in early childhood and impair functioning. Prevalence rates in the United States are reported at approximately 1%.

3.2.1.9 *ADHD*

Attention-deficit/hyperactivity disorder (ADHD) is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity that hinders functioning or development. ADHD emerges before 12 years of age. Surveys suggest that ADHD occurs in about 5% of children and about 2.5% of adults.

3.2.1.10 *Anorexia nervosa*

The main features of anorexia nervosa are persistent energy intake restriction, intense fear of gaining weight or persistent behavior that interferes with weight gain, and a disturbance in self-perceived weight or shape. The twelve-month prevalence of anorexia nervosa among young females is approximately 0.4%, debuting during adolescence or young adulthood.

3.2.1.11 *Diagnostic approach*

We applied a hierarchical approach to differentiate between schizophrenia, bipolar disorder, unipolar depression, and anxiety disorders in studies I, II, IV, and V of this thesis. Any individual with an NPR episode with one of the schizophrenia diagnoses was coded as having schizophrenia. Individuals with any diagnosis of bipolar disorder, but not schizophrenia, were regarded as having bipolar disorder. Individuals with an episode of unipolar depression, but neither schizophrenia nor bipolar disorder, was coded as having unipolar depression. Individuals with an episode of anxiety disorder but without schizophrenia, bipolar disorder, or unipolar depression were coded as having anxiety disorder. Regardless of other diagnoses, individuals with any of the

following disorders were coded accordingly: schizoaffective disorder, alcohol abuse, drug abuse, autism, ADHD, anorexia nervosa, and completed suicide. We additionally explored bipolar disorder without psychiatric comorbidity (dubbed *pure* bipolar disorder) in study IV.

In study III, we investigated schizophrenia, autism, bipolar disorder, depression, anorexia nervosa and substance abuse (including alcohol use disorder), without using a hierarchical approach; hence individuals with co-morbidity could appear in more than one category. Each disorder was first analyzed separately without accounting for co-morbidities, and then re-analyzed corrected for co-morbidities by analyzing all disorders simultaneously.

### 3.2.2 Creativity

#### 3.2.2.1 *Creative professions*

Occupation data from the Censuses were coded according to the Nordic Classification of Occupations (NYK) and the Swedish Standard Classification of Occupations (SSYK) in LISA (1983; 1998). As has been previously done, we defined scientific and artistic occupations as creative professions (Table 6) (Feist, 1998; Holland, 1997; Juda, 1949). Throughout this thesis, *creative professions* denotes the overall aggregated group of scientific and artistic occupations, while *creative occupations* is used for creative professions and for any of the subgroups (i.e., scientific and artistic). Individuals reporting a creative occupation in at least one of the mandatory Censuses were considered creative. Scientific occupations were defined as NYK code 051: University teachers, described by Statistics Sweden as individuals ‘conducting research and teaching at the university’, including occupations that commonly require active research or examination at the Ph.D. level (Statistiska centralbyrån [Statistics Sweden], 1990), but excluding researchers only active outside of the academic field.

In line with Holland’s widely used theory of vocational personalities and work environments, which considers accountants as one of the occupations with predominantly *conventional* qualities (Holland, 1997), we also defined a less creative group (accountants and auditors) to test the specificity of any associations found for creative occupations.

Authors were not delineated as a separate group in SSKYK. Therefore, information on authors was collected solely from the censuses. The Swedish term ‘författare’ used in the census is not synonymous to ‘author’ in English. The dictionary published by the Swedish Academy (the Swedish counterpart of the Oxford English Dictionary) defines ‘författare’ as ‘a person known for writing, who more or less professionally engages in writing, without further specification, but especially in terms of literary writings.’ (1927).



## MATERIALS AND METHODS

TABLE 6. DEFINITION OF CREATIVE PROFESSIONS

	NYK code <sup>a</sup>	SSYK code <sup>b</sup>
CREATIVE PROFESSIONS		
- University teachers	051	2310
- Visual artists	081	2452
- Photographers	946	3131
- Designers	082	2456
- Display artists	083	3471
- Performing artists	086	2455
- Composers and musicians	087	2453
- Choreographers and dancers	-	2454
- Authors	084	-
- Other literary and artistic work	088	-
<sup>a</sup> Nordic classification of occupations		
<sup>b</sup> Swedish standard classification of occupations		

### 3.2.2.2 *Creative Achievement Questionnaire*

The Creative Achievement Questionnaire (CAQ) is a self-reporting inventory regarding arts (drama, writing, humor, music, visual arts, and dance), science (invention, science, and cooking) and architecture (Carson, Peterson, & Higgins, 2005). Respondents answer to what amount the statements agree with their life-time creative achievements (James C. Kaufman & Sternberg, 2010). These achievements in turn refer to the amount and type of achievements spawned (e.g., for music: no recognized talent, having played one or more musical instruments, having played with a recognized orchestra, having composed an original piece of music, having been critiqued in a local publication, having a composition recorded, having recordings to be sold publicly, and having been critiqued in a national publication) (Carson et al., 2005). The results from the respective creative domains in CAQ can be individually calculated or summarized into a total score. The questionnaire has been employed in numerous studies examining creativity.

### 3.2.3 Leadership

#### 3.2.3.1 *Executive professions*

Executive professions were defined as company directors, legislators, and senior officials in public office. Individuals reporting an executive profession at least once in any of the mandatory censuses or the LISA were considered as having an executive profession.

#### 3.2.3.1.1 Political professions

Information on the subgroup of *political professions* in executive

professions was only delineated in the SSK (corresponding to the International Standard Classification of Occupations (ISCO-88) group 11). Individuals within this group 'organize, direct and is responsible for the enforcement of policy decisions; plan, direct and coordinate authorities, municipalities and counties, provide the political leadership with technical advice; represent Sweden abroad or in intergovernmental organizations, make decisions, lead and influence the activities of democratic elected bodies at national, regional or local level; decide, confirm, amend and repeal laws, regulations and administrative provisions'.

### 3.2.3.2 *Officer suitability*

In Sweden, conscription and associated assessment of cognitive ability measured as IQ was compulsory for men up until 2010, but individuals with known severe medical or psychological handicaps or living in institutions were not enrolled (approximately 2% in the early 1990s; Carlstedt, personal communication, 2011).

For those individuals with mean IQ or higher, an assessment of leadership potential, i.e., *officer suitability*, was conducted. This assessment is under 'instrument secrecy' and thus only available for members of the Swedish conscription board (Chief Psychologist Officer Lindberg; personal communication 2013). The assessments were led by board certified psychologists, where the majority of the psychologists performing the interviews had long experience of their work (Chief psychologist officer Lindberg; personal communication 2013) (Carlstedt & Widen, 1999). Traits assessed were mental stability, emotional maturity, and stress tolerance (Larsson, 1999). The interviews were semi-structured and lasted for about 20 minutes (Carlstedt & Widen, 1999). Results were presented as stanine scores ranging from 1-9, standardized against the entire conscript population with a mean of 5. Data on officer suitability is only available for males.

There is ample evidence that personality traits are relevant in the workplace (Barrick & Mount, 2005), and not least for executive professions (Hogan, Curphy, & Hogan, 1994). Validity of the semi-structured interviews of the type used in the Swedish enlistment procedure is relatively good (Carlstedt, 2006; Carlstedt & Widen, 1999). The interview in its updated form is still in use in the Swedish military and other governmental agencies (Chief Psychologist Officer Lindberg; personal communication 2013).

### 3.2.4 IQ

Two different tests of IQ were used during conscription in the studies included in this theses. The first test (1969-1994, with some updates in 1980) was based on written questionnaires, and the second (1994 and

onwards) was computer based. Both tests addressed four dimensions of the intelligence construct: logical/inductive, verbal, spatial/visual, and theoretical/technical (Gale et al., 2012; Mårdberg & Carlstedt, 1998). Results for both tests are presented as stanine scores ranging from 1-9, standardized against the entire conscript population with a mean of 5. Data on IQ was only present for males.

### 3.2.5 Heritability

Heritability provides an estimate of the proportion of genetic influences to a complex trait, ranging from 0 (no phenotypic variation due to variation in genotype) to 1 (all phenotypic variation due to variation in genotype) (Plomin, 2008). Studies of heritability often use twin and family designs, both of which have a long history dating back to Francis Galton (1869). Twin studies rely upon the fact that monozygotic (MZ) twins are genetically identical, while fraternal (dizygotic, or DZ) share on average 50 percent of their genomes identical by descent, just like ordinary full-siblings. Intra pair correlations of an investigated trait can then be used to estimate the genetic effect under the assumption that the difference of correlations in MZ-pairs compared to correlations in DZ-pairs corresponds to half of the genetic effect. Twin studies also convey two other components: shared environment that affect both twins similarly, and unshared environment, which is the unique environmental stimuli that meet one twin but not the other, or stimuli that affect each twin differently. Together these three components are abbreviated ACE, i.e., the genetic component (A), the shared environment (C), and the unshared environment (E).

In study V we explored the similarity between twins by calculating within-pair polychoric correlations of creative professions and CAQ, respectively, stratified by sex and zygosity. Outcomes were modeled via univariate liability-threshold models.

### 3.2.6 Fecundity

Fertility refers to the amount of children born per individual, which in biology is considered closely related to fecundity corresponding to the *ability* of producing offspring. Fecundity, in turn is one of the key components of biological fitness, which is crucial in natural selection. Fitness in contemporary human populations where most individuals survive past the childbearing years, is approximated by completed family size (Stearns, Byars, Govindaraju, & Ewbank, 2010).

In study III, we calculated a fertility ratio (FR) to reflect fecundity based on the number of children patients and their healthy siblings had compared to the general population, correcting for year of birth. To permit testing for sex-specific effects and avoid confounding by age

differences at parenthood and average number of children, we compared affected males to the general population of males and the same for affected females.

We further combined the FRs of affected individuals and their siblings and compared this combined prevalence of affected and siblings to that of their combined children. Thus, we combined the estimated number of children from affected individuals and their siblings, and divided by the estimated total number of children for the entire cohort.

### 3.3 STATISTICAL ANALYSES

#### 3.3.1 Linear regression

Linear regression estimates the relationship between a numerical outcome and a numerical exposure (Kirkwood, Sterne, & Kirkwood, 2003). It is used to estimate the best-fitting straight line describing the association and the correlation coefficient. Two assumptions are made in linear regression. These are 1) that the data has a normal distribution and 2) homoscedasticity.

In study **IV** we used linear regression to estimate trends based on the odds ratios for officer suitability in patients with bipolar disorder and their siblings compared the healthy controls.

#### 3.3.2 Logistic regression

Logistic regression estimates the relationship between a categorical (binary or ordinal) outcome and both categorical and numerical exposures (Kirkwood et al., 2003). It is often used to estimate the relation between exposure and a binary outcome (e.g., case-control), while potential confounders are being controlled for. Logistic regression provides an odds ratio (OR), i.e., the odds of being a case compared to control. For rare outcomes the OR is roughly equivalent to relative risk. Assumptions made for logistic regression is that the relationship between the outcome and the exposure is linear on the logit scale for numerical variables and that the distribution of the residuals is normal. In case-control studies where controls are individually matched, *conditional* logistic regression is generally the most suitable method. This method obtains unbiased estimates of coefficients of interest.

We used conditional logistic regression in study **I**, **II**, and **IV** to estimate the associations for occupations across each class of patients and relatives.

#### 3.3.3 Generalized estimating equation

If data are clustered, i.e., observations in one cluster tend to be more similar to each other than to individuals in the rest of the sample, then this need to be allowed for in the analysis (Kirkwood et al., 2003).

Failure to account for clustering may lead to standard errors of estimates being too small and therefore confidence intervals to narrow. Generalized estimating equations (GEE) modify both parameter estimates and standard errors to allow for clustering.

In study III, we used GEE to estimate a fertility ratio for patients and their healthy siblings in comparison with the general population.

#### 3.3.4 Structural equation modelling

The term Structural equation modeling (SEM) does not designate a single statistical technique but instead refers to a family of related procedures (R. B. Kline, 2011). SEM requires a priori information about aspects such as which variables are assumed to affect other variables and the directionalities of these effects. These a priori specifications make up the model to be analyzed. SEM therefore requires a fundamental knowledge of the theoretical and empirical literature in the research area investigated. This is because everything from the design of the initial model, over the adjustment of that model in subsequent reanalyses, to interpretation of the results must be led by knowledge in the domain investigated.

SEM may be used in a *strictly confirmatory* way, where a single model is accepted or rejected based on the data. However, it is seldom that the researcher will be satisfied with this. SEM is more often used to test *alternative models*, and even more often for *model generation*, when an initial model does not fit the data and is subsequently modified by the researcher. The altered model is then tested again with the same data. The goal of this process is to find a model with three basic properties: 1) making theoretical sense, 2) being reasonably parsimonious, and 3) corresponding acceptably close to the data.

The fit of the model in relation to the data can be tested with different methods. In study V we used the Akaike information criterion (AIC) when investigating the heritability of creative professions and creative achievement. AIC provides a trade-off between the goodness of fit of the model and the complexity of the model (Burnham & Anderson, 2004).

### 3.4 STUDY DESIGNS

#### 3.4.1 Study I

We used a nested case-control design to study associations between having a creative occupation and being diagnosed with schizophrenia, bipolar disorder, or unipolar depression or being a 1<sup>st</sup>-, 2<sup>nd</sup>-, or 3<sup>rd</sup>-degree relative of these patients. Ten control subjects matched on sex and birth year were randomly selected from the MGR for each patient and each of their relatives. To assess the association between a creative

occupation across each class of patients and relatives, we estimated odds ratios using conditional logistic regression. Since several correlated pairs of relatives from every family could be included in an analysis, a robust sandwich estimator was used to adjust for the correlated data when calculating the confidence intervals. To determine whether IQ mediated the association between creativity and psychopathology, it was included as a continuous covariate in the regression model.

To further investigate the familial effect, we examined the rates of creative occupations in non-affected half siblings of patients who shared either a mother (maternal half siblings) or a father (paternal half siblings). The rationale for this comparison is that maternal half siblings are exposed more to common environments than are paternal half siblings, but are equally genetically related (on average 25%); that is, not only have maternal half siblings been exposed to a similar intrauterine environment, it has also been observed that 91% of children stay with their mother after a divorce (1994). Thus, if creative occupations were more common in maternal half siblings compared to paternal half siblings, this would suggest that early environmental factors are important in determining creativity (Lichtenstein et al., 2009).

#### 3.4.2 Study II

We used a similar design as in study I in a considerable larger cohort, including schizoaffective disorder, anxiety disorders, alcohol abuse, drug abuse, autism, ADHD, anorexia nervosa, and completed suicide to estimate the occurrence of creative occupations in patients and their first-, second-, and third-degree relatives compared to non-diagnosed controls.

To specifically consider authors, this group was investigated as a separate group.

#### 3.4.3 Study III

We conducted a study where all individuals born 1950-1970 in Sweden were included. The average number of children among included patients diagnosed with schizophrenia, autism, bipolar disorder, depression, anorexia nervosa or substance abuse (including alcohol use disorder) and their healthy siblings was compared to the general population, accounting for age, sex and family size.

Data were analyzed using generalized estimating equation. The resulting FR was further used to combine the estimated number of children from affected individuals and their siblings, and then subsequently divided by the estimated total number of children for the entire 1950-1970 birth cohort. This provided an estimation of the prevalence of offspring to patients and their siblings in relation to the offspring of the general population. The main reason for this was to try to

investigate if traits associated with the different psychiatric disorders included are under positive or negative selection.

#### 3.4.4 Study IV

We analyzed officer suitability, and executive and political professions in bipolar patients with and without comorbidity and in their healthy siblings compared to controls with conditional logistic regression. In the analysis of officer suitability, the standardized mean of 5 was used as reference, and odds ratios were then estimated for every other value of officer suitability in cases (patients and their siblings) compared to controls. Ten control subjects matched on sex and birth year were randomly selected from the MGR for each patient and each of their relatives. A robust sandwich estimator was used to adjust for correlated data when calculating the confidence intervals. Results were additionally adjusted for IQ (men only). In addition, P-values for linear and quadratic trends were analyzed based on the odds ratios for officer suitability.

#### 3.4.5 Study V

We systematically reviewed previous research on the genetics of creativity and performed two twin studies of heritability based on creative professions in national censuses, and CAQ in SALTY, respectively.

The systematic review was based on the Prisma Statement methodology. We used the search algorithm (*creativity OR creativeness*) AND (*familiarity OR heritability OR genes OR genetics OR genome*) to collect articles from PubMed, the Web of Science, and PsychINFO. High quality studies were defined as those with a 'valid definition of creativity, comparative study design, adequate statistical analysis and power'.

The two new original studies on heritability of creative professions and CAQ were performed using structural equation modeling. We explored the similarity between twins by calculating within-pair polychoric correlations of the outcome measure, stratified by sex and zygosity. Outcomes were modeled via univariate liability-threshold models. If the initial correlations indicated it, sex-limitations were included in the model.

## 4 Results



## RESULTS

### 4.1 STUDY I

We identified 54 042 people (29 479 males and 24 563 females) with schizophrenia, 29 644 people (11 910 males and 17 734 females) with bipolar disorder and 217 771 people (84 352 males and 133 419 females) with unipolar depression.

#### 4.1.1 Schizophrenia

Compared with the control group, those with schizophrenia (OR = 0.98, 95% CI 0.88–1.08) demonstrated no difference in having a creative profession, but showed a significantly decreased likelihood of holding a scientific occupation (OR = 0.63, 95% CI 0.51–0.79). There was also a significant increase in the likelihood of holding an artistic occupation (OR = 1.14, 95% CI 1.01–1.28), which in turn was mainly as a result of an increase in visual artistic occupations (OR = 1.30, 95% CI 1.13–1.49).

Parents and siblings of people with schizophrenia were significantly more likely to hold a creative profession compared with the control group (OR<sub>Parents</sub> = 1.55, 95% CI 1.43–1.67; OR<sub>Siblings</sub> = 1.36, 95% CI 1.26–1.48). This increase was present across all creative domains.

#### 4.1.2 Bipolar disorder

Individuals with bipolar disorder were significantly overrepresented in creative professions compared with the control group (OR = 1.35, 95% CI 1.22–1.48). This was primarily because of an increased likelihood of both visual (OR = 1.42, 95% CI 1.23–1.64) and non-visual (OR = 1.44, 95% CI 1.20–1.73) artistic occupations.

First-degree relatives of those with bipolar disorder were more likely than those in the control group to hold a creative profession in general, with higher odds ratios for scientific than artistic occupations.

#### 4.1.3 Unipolar depression

Individuals with unipolar depression showed no increased rate of overall creative professions (OR = 0.94, 95% CI 0.90–0.99). Similarly, there was no consistent pattern with respect to the frequency of creative occupations in relatives of those with unipolar depression.

#### 4.1.4 Accountants and auditors

People with bipolar disorder and their first-degree relatives generally displayed no significant associations with accountants and auditors, whereas those with schizophrenia or unipolar depression and their first-degree relatives generally displayed significant decreases in the likelihood of holding such an occupation.

#### 4.1.5 Half-siblings and IQ

We found no consistent pattern of differences between maternal and paternal half-siblings (creative professions maternal vs. paternal: schizophrenia (OR 1.26, 95% CI 0.91–1.74) v. (OR 1.08, 95% CI 0.82–1.41); bipolar disorder: (OR 1.21, 95% CI 0.75–1.94) v. (OR 1.03, 95% CI 0.71–1.49); unipolar depression: (OR 0.81, 95% CI 0.66–1.00) v. (OR 0.98, 95% CI 0.85–1.14)).

We found that IQ (men only) was generally higher in people with creative occupations, but lower in those with schizophrenia, bipolar disorder, unipolar depression and their respective relatives compared with people without any of the three diagnoses. To determine whether IQ mediated the association between creativity and psychopathology, it was included as a continuous covariate in the regression model. As a result, however, the associations were strengthened rather than attenuated.

## 4.2 STUDY II

We identified 65 589 patients (35 819 men and 29 770 women) with schizophrenia, 14 905 individuals (6 145 men and 8 760 women) with schizoaffective disorder, 68 915 (27 199 men and 41 716 women) with bipolar disorder, and 438 372 patients (170 781 men and 267 591 women) with unipolar depression. Further, 212 758 patients (84 087 men and 128 671 women) were diagnosed with anxiety disorders, 340 784 (246 905 men and 93 879 women) with alcohol abuse/dependence, 136 490 (80 303 men and 56 187 women) with drug abuse/dependence, 11 802 (8 281 men and 3 521 women) with autism, 48 024 (32 973 men and 15 051 women) with ADHD, 17 276 (2 384 men and 14 442 women) with anorexia nervosa, and 73 766 persons (52 516 men and 21 250 women) that died from completed suicide.

#### 4.2.1 Creative professions

We found no positive association between overall creative professions and psychopathology except for bipolar disorder. Rather, individuals holding creative professions had a significantly reduced likelihood of being diagnosed with schizophrenia, schizoaffective disorder, unipolar depression, anxiety disorders, alcohol abuse, drug abuse, autism, ADHD, or of committing suicide.

#### 4.2.2 Authors

Authors suffered from schizophrenia and bipolar disorder more than twice as often as controls. Authors were also more likely to be diagnosed with unipolar depression, anxiety disorders, alcohol abuse, drug abuse, and to commit suicide. The finding of increased risk for suicide in authors might be secondary to other psychopathology.

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To investigate this further, we omitted all authors with any psychiatric diagnosis in the NPR (ICD-8: 290-315, ICD-9: 290-319, ICD-10: F00-F99). There was still a trend for authors without diagnosed psychopathology to commit suicide more frequent than controls (OR 1.45, 95% CI 0.97-2.16;  $p = 0.07$ ). Thus, regardless of psychopathology, being an author seemed to increase suicide risk.

### 4.2.3 Relatives

Compared to study I, the inclusion of additional patients and data on creative occupations did not change the familial association between schizophrenia and bipolar disorder and creative professions. Patients' first-degree relatives were still significantly overrepresented in these professions. In addition, we found associations between creative professions and being a sibling of individuals with autism and being parent or sibling of individuals diagnosed with anorexia nervosa.

### 4.2.4 Accountants and auditors

In general, being an accountant meant negative or no association to the psychopathologies investigated in this study.

### 4.2.5 IQ

IQ (available for men only) was generally higher in people with creative occupations, but lower in patients with the psychiatric disorders studied and their respective relatives compared to people without these diagnoses. Including IQ as a continuous covariate in the regression model resulted in that the crude overrepresentations were generally strengthened rather than attenuated.

## 4.3 STUDY III

The mean (SD) number of children for the birth cohort was 1.76 (1.27). Because only minor differences were observed between the adjusted and non-adjusted estimates, only the adjusted estimates are presented herein.

### 4.3.1 Schizophrenia

Individuals with schizophrenia had fewer children compared with the general population, with FRs of 0.23 (95% CI, 0.23-0.24) for men and 0.47 (95% CI, 0.46-0.48) for women. Sisters of affected individuals had a significantly increased number of children (FR, 1.02; 95% CI, 1.01-1.03), while brothers of affected individuals showed significantly decreased fecundity (FR 0.97, 95% CI 0.96-0.99). When comorbidities were included in the analysis, the increased fecundity in sisters disappeared.

#### 4.3.2 Autism

Both men (FR 0.25, 95% CI 0.23-27) and women (FR 0.48, 95% CI 0.44-0.51) with autism had significantly fewer children. Brothers of affected individuals also had fewer children (FR 0.94, 95% CI 0.90-0.97), while sisters of affected individuals showed no significant difference from the general population. These results did not differ significantly when comorbidities were included in the analysis.

#### 4.3.3 Bipolar disorder

Men and women with bipolar disorder had fewer children than the general population (male FR 0.75, 95% CI 0.73-0.77; female FR 0.85, 95% CI 0.84-0.87). Brothers of affected individuals showed no significant difference from the general population, while sisters of affected individuals had an increased number of children (FR 1.03, 95% CI 1.02-1.05). When correcting for comorbidity, the increased fecundity in sisters disappeared, and the reduced fecundity in affected individuals increased to just below that of the general population (male FR 0.94, 95% CI 0.92-0.96; female FR 0.95, 95% CI 0.93-0.97).

#### 4.3.4 Unipolar depression

Men with unipolar depression had fewer children (FR 0.93, 95% CI 0.92-94), but women with depression showed no significant difference from the general population. Siblings of affected individuals had more children compared with the general population (brothers' FR 1.01, 95% CI 1.01-1.02; sisters' FR 1.04, 95% CI 1.03-1.05). This increased fecundity in siblings remained when comorbidities were accounted for, although the reduced number of children among affected men disappeared and the fecundity among women with unipolar depression increased (FR 1.03, 95% CI 1.03-1.04).

#### 4.3.5 Anorexia nervosa

Individuals with anorexia nervosa had a reduced number of children (male FR 0.54, 95% CI 0.48-0.62; female FR 0.81, 95% CI 0.79-0.84). Neither the fecundity of brothers nor sisters differed from that of the general population. These results did not change after correction for comorbidities.

#### 4.3.6 Substance abuse

Men having a diagnosis of substance abuse had significantly fewer children than the general population (FR 0.78, 95% CI 0.78-0.79), as did women having a diagnosis of substance abuse (FR 0.92, 95% CI 0.91-0.93). Siblings of individuals with substance abuse had more children than the general population, with FRs of 1.03 (95%

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CI 1.02-1.04) for brothers and 1.05 (95% CI 1.05-1.06) for sisters. These values did not differ significantly when comorbidities were included.

### 4.4 STUDY IV

We identified 22 980 patients (9 548 men and 13 432 women) with pure bipolar disorder (without comorbidity) and 68 915 patients (27 199 men and 41 716 women) with general bipolar disorder (with and without comorbidity).

#### 4.4.1 Officer suitability

Patients (men only) with pure bipolar disorder were overrepresented in both the highest and lowest stanine strata of assessed officer suitability ( $OR_{\text{highest}} 1.46$ , 95% CI 1.02-2.08;  $OR_{\text{lowest}} 1.56$ , 95% CI 1.02-2.36). Similar, but less pronounced, estimates were found in their healthy brothers ( $OR_{\text{highest}} 1.37$ , 95% CI 1.06-1.78;  $OR_{\text{lowest}} 1.26$ , 95% CI 0.88-1.79).

Patients (men only) with general bipolar disorder were not overrepresented in the group with highest officer suitability but only in the group with lowest officer suitability ( $OR_{\text{highest}} 1.07$ , 95% CI 0.86-1.34;  $OR_{\text{lowest}} 2.95$ , 95% CI 2.43-3.57).

#### 4.4.2 Executive professions

Patients (both genders) with pure and general bipolar disorder were underrepresented in executive professions ( $OR_{\text{pure}} 0.58$ , 95% CI 0.53-0.63;  $OR_{\text{general}} 0.43$ , 95% CI 0.41-0.45; Table 4). By contrast, siblings of patients with pure bipolar disorder were overrepresented in executive professions (OR 1.08, 95% CI 1.02-1.15). This was particularly pronounced in the political subgroup of executive professions (OR 1.85, 95% CI 1.25-2.75).

#### 4.4.3 IQ

Males with executive professions had higher mean IQ compared to the entire conscript population (data not shown), whereas males with pure bipolar disorder had similar IQ (5.22, 95% CI 5.14-5.30) as those without a psychiatric diagnosis (5.16, 95% CI 5.16-5.16). Males with general bipolar disorder, however, had lower IQ (4.79, 95% CI 4.75-4.83) than those without a psychiatric diagnosis.

Adjusting crude results for those individuals with data on IQ present slightly attenuated point estimates. However, this led to pure bipolar patients with data on IQ (Crude: OR 1.47, 95% CI 1.03-2.09,  $p=0.03$  vs. Adjusted for IQ: 1.44, 95% CI 1.00-2.07,  $p=0.05$ ) and their siblings (Crude: OR 1.37, 95% CI 1.06-1.79,  $p=0.02$  vs. Adjusted for IQ: OR 1.26, 95% CI 0.96-1.65,  $p=0.10$ ) no longer being significantly overrepresented in superior strata of officer suitability. Similarly, siblings to patients

with pure bipolar disorder were not significantly overrepresented in executive professions (Crude: OR 1.00, 95% CI 0.90-1.11,  $p=0.97$  vs. Adjusted for IQ: OR 0.95, 95% CI 0.85-1.06,  $p=0.34$ ) and political professions (Crude: OR 1.69, 95% CI 0.75-3.80,  $p=0.21$  vs. Adjusted for IQ: OR 1.52, 95% CI 0.69-3.37,  $p=0.30$ ). The latter likely due to loss of power.

## 4.5 STUDY V

### 4.5.1 Systematic review

A total of 56 studies were included in the review. In general, results regarding the genetics of creativity were conflicting both across and within studies of this review. Of the included studies 48 demonstrated positive findings of familiarity or a specific genetic component, 6 demonstrated conflicting results, while 2 demonstrated negative results. Thus, 86% of studies demonstrated positive results, while 14% demonstrated conflicting or negative results. In *high quality* twin studies reporting positive results ( $n=6$ ), estimations of heritability ranged from 0.22 (Nichols, 1978) to 0.78 (Barron, 1970).

### 4.5.2 National study of the heritability of creative professions

We included 35 339 complete twin pairs from the STR. A total of 2 282 (3.2%) of the included twins held a creative profession.

Both male and female monozygous twins showed significant and comparable correlations (males:  $R$  0.62, 95% CI 0.54-0.70; females:  $R$  0.59, 95% CI 0.50-0.67). The correlations for the corresponding dizygous pairs were substantial, but significantly lower than for the monozygous pairs (males:  $R$  0.45, 95% CI 0.35-0.55,  $p\leq 0.01$ ; females:  $R$  0.27, 95% CI 0.13-0.28,  $p\leq 0.01$ ). The correlation between opposite-sex twins was close to female dizygous pairs ( $R$  0.28, 95% CI 0.19-0.35) and significantly different from the correlation for male dizygous pairs ( $p\leq 0.02$ ). Thus, raw correlations indicated a) statistically significant heritability for both males and females, b) differences between sexes.

In the final simplified model we excluded the shared environment component for females. Females in this final model thus demonstrated an AE pattern (A: 58%, E: 42%), while males demonstrated an ACE pattern (A: 42%, C: 21%, E: 37%). Thus the heritability (A) for creative professions in females was higher than in males, who instead demonstrated an unusually high estimate of shared environment (C).

### 4.5.3 Twin study of creative achievement

A total of 3 070 twins choose to participate in the web survey including CAQ in SALTY. Of these, there was 391 complete pairs of twins (i.e., 782 individuals).

We found that for male pairs, the correlation was almost identical

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for monozygous (R 0.33, 95% CI 0.01-0.59) and dizygous (R 0.35, 95% CI 0.04-0.52) twins, indicating that the similarity between male twins could be explained by shared environment (C) alone. For female pairs on the other hand we found that the correlation for monozygous pairs (R 0.59, 95% CI 0.41-0.74) was higher than for dizygous pairs (R 0.38, 95% CI 0.17-0.56), though not statistically significantly so ( $p=0.13$ ). On the other hand, we found that opposite-sexed twins were almost completely uncorrelated (R 0.02, 95% CI -0.20-0.25), suggesting that whatever mechanism allows for significant similarity within same-sexed pairs does not work for mixed pairs, i.e., the difference in correlation between female pairs and mixed pairs was statistically significant ( $p\leq 0.03$ ). Thus, raw correlations suggested considerable differences between sexes, with no or little heritability for males, while allowing for heritability in females.

Females in the final model demonstrated an AE pattern (A: 62%, E: 38%), while males demonstrate a CE pattern (C: 33%, E: 67%). Thus, there was considerable heritability (A) for CAQ in females similar to that of the heritability for females in creative professions, while males demonstrated practically no heritability at all for CAQ, but again an unusual high estimate of shared environment (C).

## 5 Discussion



## 5.1 SUMMARY OF FINDINGS

### 5.1.1 Psychotic and mood disorders

There is consistency in findings of studies on psychotic and mood disorders in relation to creativity. First, none of the studies included in the literature review have indicated increases in general creative abilities in patients with schizophrenia. In study I we demonstrated a specific increase in artistic occupations in patients with schizophrenia, but we were unable to validate these findings in the larger sample investigated in study II.

Second, in contradistinction to studies on patients with schizophrenia, all included studies reviewed reported associations between different aspects of creativity and subsyndromal psychotic symptoms, i.e., psychoticism and schizotypy. Two studies pointed out, however, that schizotypy was mainly associated with self-reported capacities to be creative (G. F. Miller & Tal, 2007; Schuldberg, 2005). Miller et al. suggested that the increase in verbal and drawing creativity was mainly due to a correlated increase in Big Five personality trait openness to experience. However, other authors have commented that this interpretation is based on the assumption that the effect of openness to experience has to be partialled out from that of schizotypy, while the data are equally consistent with, e.g., a path model where openness to experience fully mediates the effect of schizotypy on creativity (i.e., schizotypy increases openness to experience, which in turn augments creativity) (Marco Del Giudice, Angeleri, Brizio, & Elena, 2010). In line with the findings on subsyndromal symptoms being associated with creativity, studies also affirm an association for non-diagnosed relatives of patients. In study I and II we could affirm an overall association for healthy relatives of patients with schizophrenia (and bipolar disorder) for creative professions. The results of these studies suggest an underlying genetic explanation for the association of creativity and psychotic disorders. In study V we affirm a general genetic component in creativity contingent on sex.

Third, many studies, including study I and II of this thesis, support that patients with bipolar disorder have increased creative abilities, a finding also present in their non-diagnosed relatives. Some studies also affirm a similar association for the affective temperament. Fourth, the association between unipolar depression and creativity is more ambiguous. Studies investigating prominent individuals (i.e., big-C) have pointed to an increase in depression. However, most studies investigating patients with major depressive disorder, including study I and II of this thesis, do not indicate increased creative ability. Similar negative findings are also evident in relatives to these patients.

### 5.1.1.1 *Leadership and bipolar disorder*

There is limited empirical support for an association between leadership traits and bipolar disorder. Study IV, however, demonstrated that patients with bipolar disorder without comorbidity (*pure* bipolar disorder) were overrepresented in both the highest and lowest strata of officer suitability ratings. Similar but less pronounced estimates were found in their healthy siblings. Patients with pure bipolar disorder were underrepresented in executive professions, whereas their siblings were overrepresented in these professions. This overrepresentation was particularly pronounced in the subgroup of political professions. These results suggest that traits related to bipolar disorder, rather than bipolar disorder *per se*, are associated with superior leadership qualities.

### 5.1.2 Neurodevelopmental disorders

Far fewer studies have investigated a possible link between creativity and neurodevelopmental disorders, than with psychotic and mood disorders. While distinguished researchers such as Michael Fitzgerald and Simon Baron-Cohen have clearly argued for a relation between autism and exceptional achievements, mainly in terms of a greater aptitude for scientific activities, the empirical support is much weaker (Baron-Cohen, Ashwin, Ashwin, Tavassoli, & Chakrabarti, 2009; Fitzgerald, 2004). Often historical examples, such as Ludwig Wittgenstein, are referenced in support for the hypothesis (Fitzgerald, 2004). Empirical support has also been provided in a few studies of non-diagnosed relatives of patients with autism (Baron-Cohen et al., 1998; Campbell & Wang, 2012). No study has shown that autism itself would be beneficial for creativity. Similarly in ADHD/ADD, where there have also been suggestions of increased creativity; empirical support is limited. Studies included in the review generally give no such support among children with ADHD/ADD, but support is provided in a few studies of adults with ADHD/ADD and possibly among those with subclinical syndromes (Healey & Rucklidge, 2006; White & Shah, 2006, 2011). Our studies (I and II) give little support for an association of ADHD/ADD or autism with creative professions, albeit non-diagnosed siblings of patients with autism were overrepresented in overall creative professions (study II). This increase was especially pronounced in the subgroup of scientific occupations. However, both parents and offspring to patients in this study demonstrated no comparable overrepresentation in creative professions. The suggestion that children with learning disability disorders are superior to their peers in creative abilities is in the main not supported empirically.

### 5.1.3 Substance use/abuse

Some conclusions can be drawn from the studies reviewed. First, acute alcohol intoxication has a positive effect on creative thinking. Results affirm increased divergent thinking, but also a more positive evaluation of subjects with regards to their own creativity. The latter might not be due to the pharmacological effects of alcohol, but rather that people apply more lenient standards to evaluation of their creativity when they believe to be intoxicated (Lang et al., 1984). Second, studies (including study II) suggest that alcohol abuse in the long run is not beneficial for creativity. Third, there does not seem to be a familial pattern that associates alcohol abuse with creativity. Finally, the acute effects of other drugs on creative performance are under researched. Long term consequences of drug abuse is likely not beneficial for creativity (study II).

### 5.1.4 Neurological disorders

Studies on creativity and neurological disorders can be seen in relation to the recent surge of studies investigating the neural underpinnings of the creative process. For a thorough discussion on these topics the reader is referred to other reviews (Dietrich & Kanso, 2010). In essence, there is little empirical support that any neurological disorder might facilitate a sustained increase in creativity.

### 5.1.5 Other mental disorders

Of studies on mental illnesses that do not fall into any of the categories reviewed above, some suggest an increased occurrence of anxiety disorders, behavioral problems, and affective vulnerability. Study I suggested a small increase of anxiety disorders in artistic occupations. On the other hand, Smith et al. concluded that the main hindrance to creative functioning is low tolerance of the anxiety accompanying creative efforts (Smith & Carlsson, 1983).

There is conflicting results regarding suicide and creativity. Study II did not provide any support for an increase of suicide in overall creative professions. However, as in many previous studies authors singled out having a significant increase in most psychiatric disorders as well as in suicide. In general these increases revealed no familial pattern.

### 5.1.6 Heritability of creativity

Study V comprised a systematic review on the genetics of creativity and two new original studies on the heritability of creativity. Focusing on the 10 twin studies of creativity reviewed and considered with high quality; 6 showed positive results, while 3 demonstrated conflicting results and 1 had negative results. In the high quality twin studies

reporting positive results ( $n=6$ ), estimations of heritability ranged from 0.22 (Nichols, 1978) to 0.78 (Barron, 1970).

These results are in line with our two new original studies (study V) on creative professions and the CAQ, respectively. Both these studies are large in comparison with previous twin studies performed in the area. In our two studies, we report a 60/40 split between the genetic component (A) and the unshared environmental component (E) for females in both creative professions and CAQ. In males, however, the genetic component was considerably smaller ranging from roughly 40% in creative professions to being non-existent in CAQ. In males, but not in females, there was also a substantial and similar shared environmental component (C) in creative professions and CAQ.

#### 5.1.7 Fecundity in psychopathology

Results from study III demonstrated that except for women with depression, investigated patients had significantly fewer children than the general population. This reduction was consistently greater among men than women. Although sisters of patients with schizophrenia and bipolar disorder had increased fecundity, this was too small on its own to counterbalance the reduced fecundity of affected patients. Brothers of patients with schizophrenia and autism showed reduced fecundity. Siblings of patients with depression and substance abuse had significantly increased fecundity. In the case of depression, this more than compensated for the lower fecundity of affected individuals.

In general the findings in study III is in line with extensive earlier research on schizophrenia (Keller & Miller, 2006; Uher, 2009), but differ somewhat with regards to many of the other disorders investigated. For example in bipolar disorder, fecundity of affected patients was just below that of the general population. This agrees with the results of another study of affective psychosis in Sweden (MacCabe, Koupil, & Leon, 2009), but disagrees with other studies (Howard, Kumar, Leese, & Thornicroft, 2002; Laursen & Munk-Olsen, 2010; Slater, Hare, & Price, 1971). It has been suggested that the introduction of lithium has led to improved functioning in patients with bipolar disorder and, as a consequence, greater fecundity in those populations where treatment is available (Surja & El-Mallakh, 2007).

## 5.2 METHODOLOGICAL CONSIDERATIONS

While numerous authors have contributed with significant work on the alleged association between creativity and psychopathology, research in this area has been hindered by an overly reliance on biographical data and small cohorts (Schlesinger, 2009). The aim of this thesis was therefore to use large scale epidemiological methodology to provide a solid empirical basis for an informed opinion on the matter.

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Nevertheless, the methodology used in this thesis is open for some important considerations.

The main aim for epidemiological studies is to assert exposure effects on outcomes. Golden standard in this regard is the *randomized experiment*, where the exposure can be randomized to study participants. However, for obvious practical and ethical reasons, the randomized experiment is not always an option. Randomized controlled trials (RCTs), a common experimental design in epidemiological research may also be hampered by strict inclusion criteria, resulting in low generalizability. Many times *observational studies* are therefore used to investigate correlations. All studies (I-V) included in this thesis are observational. The disadvantage with this approach is that causal inference is not possible, and that unidentified factors may lead to biased results.

For that reason *quasi-experimental designs* (QEDs) offers an interesting alternative. Family-based, quasi-experimental designs reduces genetic and environmental confounding, thereby providing indication of causality (study I and V). Another option is to use *negative control analyses* to get an indication of the influence of confounding. Study I and II included *accountants and auditors*, a less creative occupational group, as a negative control. This provided an opportunity to investigate the effects of having an occupation in general - importantly as a group accountants and auditors also demonstrated a similar IQ mean as the overall creative professions.

### 5.2.I Internal validity

Internal validity refers to the extent that a study can rule out or make unlikely alternate explanations of the results. The results of the analyses in this thesis may be subjected to two major kinds of deficiency in internal validity, systematic errors (i.e., selection bias, information bias and confounding) and random errors (i.e., caused by chance). While systematic errors can be handled by the investigator, random errors are not open for correction, but are reduced with increasing sample size or by decreasing the variability in measurement.

#### 5.2.I.I Selection bias

Selection bias is the result when study subjects are selected as a result of an unknown variable associated with both the exposure and outcome investigated.

#### 5.2.I.I.I Professions, officer suitability, and CAQ

Study I, II, IV, and V collected data on professions from the national censuses and LISA. In study I, II, and IV we compared non-response rates regarding occupation among those with a psychiatric diagnosis (cases), their healthy siblings and controls.

Study I demonstrated that those in the case group had higher rates of missing data than their respective controls, whereas healthy siblings of those in the case group had similar rates of missing data compared with their respective controls. To understand how missing data status influenced the associations, we compared the prevalence of creative professions in siblings of those in the case group with or without missing data on occupation. Siblings of people with schizophrenia with a missing value significantly more often had creative professions compared with siblings of those with schizophrenia with a valid occupation. The opposite was true for siblings of people with unipolar depression. No significant differences were found in siblings of those with bipolar disorder.

Study II again demonstrated that patients had higher rates of missing data than their respective controls, whereas healthy siblings of patients had similar rates of missing data compared to their respective controls. Comparing the prevalence of creative professions in siblings of patients with or without missing data on occupation showed that siblings of schizophrenic patients and siblings of persons with completed suicides with a missing value, had creative professions more often than siblings of patients with a valid occupation. The opposite, i.e., less often creative professions, was true for siblings of patients with bipolar disorder, unipolar depression, anxiety disorders, alcohol abuse, drug abuse, and ADHD. No significant differences were found in siblings of patients with schizoaffective disorder, autism, or anorexia nervosa.

Study IV found more missing occupational data, i.e., missing, un-specific, or unemployed in patients with general bipolar disorder than in their respective controls, while their healthy siblings had more similar rates of missing data compared to their respective controls.

Officer suitability measurements in study IV were restricted to men with an IQ mean of  $\geq 5$ . The use of CAQ in study V may have introduced selection bias due to possible systematic differences between responders and non-responders. The narrow definition of scientific occupations used in study I and II could possibly result in selection bias. Scientific occupations were defined as NYK code 051: University teachers, described by Statistics Sweden as individuals 'conducting research and teaching at the university', including occupations that generally require active research or examination at the Ph.D. level, but excluding researchers only active outside the academic field.

The general use of artistic and scientific occupations as a proxy for creativity in study I, II, and V could constitute selection bias, considering the many different ways to measure creativity (James C. Kaufman, Plucker, & Baer, 2008). But, while creativity could be assumed to be an essential part in many different occupations and areas of life, it has

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been argued that creativity is at the core of artistic and scientific occupations (Florida, 2002).

### 5.2.1.1.2 Psychiatric diagnoses

Swedish health care is publicly funded and Swedish health registers are essentially complete (Ludvigsson et al., 2011). Relevant for all studies of this thesis, but especially for study IV, however, is that it is possible that persons with executive professions in Sweden could seek psychiatric care exclusively in other countries. These individuals would thereby circumvent inclusion in this study resulting in selection bias. Still, most of these individuals would probably engage in outpatient care abroad, while inpatient care would be received in Sweden due to urgency of treatment. These individuals would consequently still be included in this study.

### 5.2.1.1.3 Left truncation and right censoring

All studies in this thesis (I – V) use register data that could introduce selection bias due to left truncation (lack of information before register start) and right censoring (inability to follow individuals after the end of register follow-up). We dealt with these limitations by matching on birth year to make certain that cases and controls had equivalent time at risk to enter registers and equal time at register follow-up.

### 5.2.1.2 *Information bias*

Information bias refers to bias arising from measurement error (Rothman, 2012). This may lead to misclassifications of outcome and exposure resulting in false associations (type I error) or false negatives (type II error). Misclassification that is similar (non-differential) across groups (exposures, outcomes, and covariates) results in a diluted effect, while differential misclassification results in an overestimation or underestimation of effect. A common reason for information bias is *recall bias*. Information bias is therefore generally reduced in prospective designs. All studies (I-V) included in this thesis used prospectively collected data.

### 5.2.1.2.1 Professions, officer suitability, and CAQ

Occupational information in the Swedish censuses has been investigated by comparing survey data from personal interviews in 1977 and 1979-1981 to 1980 Census data, suggesting good agreement between the two sources (i.e., NYK 1-digit level: ~90%; 2-digit level: ~80%; 3-digit level: ~70%) (Wärneryd, Thorslund, & Östlin, 1991).

The assessment battery for officer suitability was initially based on research collected during the Korean war and successively refined and validated (Chief psychologist officer Lindberg; personal

communication 2013). Inter-rater reliability was analyzed consistently. The conscription board accepted no more than a one point difference in agreement among raters.

CAQ has been validated by Carson et al. reporting acceptable results concerning reliability and validity (Carson et al., 2005). Study V used an unvalidated Swedish translation of the CAQ. Two creative domains were dropped, i.e., *architectural design* and *humor*, and the scores for the remaining domains were changed from 0–7 to 0–6.

#### 5.2.1.2.2 Psychiatric diagnoses

Inpatient diagnoses of schizophrenia from the NPR have good to excellent validity, with 94% agreement when compared to research diagnoses, based on semi-structured interviews and medical records (Ekholm et al., 2005). The validity of schizoaffective disorder has not been investigated in the NPR, however, one study found that 86% (i.e., 6 of 7 patients) with an ICD-8 diagnosis of schizoaffective disorder (295.70) in the NPR did not fulfill the DSM-III criteria for schizophrenia when investigated through medical records (Kristjansson, Allebeck, & Wistedt, 1987). The validity of bipolar disorder in the NPR has recently been addressed, with a positive predictive value of 0.81–0.92 relative to diagnostic status based on patients' medical records (Sellgren, Landen, Lichtenstein, Hultman, & Langstrom, 2011). The validity of a single depressive episode in the Danish national psychiatric register has demonstrated sufficient precision for clinical practice, with increasing validity correlated to increasing severity (65–83%) (Bock, Bukh, Vinberg, Gether, & Kessing, 2009). To our knowledge, no studies have been published on the validity of unipolar depression, anxiety diagnoses, anorexia nervosa, or ADHD in the Swedish NPR. Autism diagnosis was investigated in the Finnish Hospital Discharge Register, suggesting that 96% of subjects with register diagnoses of childhood autism fulfilled criteria based on the ADI-R inventory (Lampi et al., 2010). The validity of alcohol abuse was also addressed in the Finnish Hospital Discharge Register by Kesimäki et al. demonstrating 98% accuracy compared to medical records (1991). Official data of suicide and attempted suicide has often been used in major studies, however, also questioned (Nordentoft, 2007; Tidemalm, Langstrom, Lichtenstein, & Runeson, 2008). Although we are not aware of any study that has investigated the validity of suicide specifically in the CDR, one study investigating 68 deaths of patients with schizophrenia that were registered under 'external causes of injury and poisoning' according to ICD in the Stockholm County inpatient register, found seven suicides that were misclassified as 'accidents' or 'undetermined' (Allebeck, Varla, & Wistedt, 1986).



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### 5.2.1.3 *Confounding*

A confounder is a variable associated with both exposure and outcome resulting in a spurious association. Experimental studies may randomize participants in order to handle possible confounding, however, observational studies does not have that alternative. Therefore, matching or stratification is often used to deal with possible confounding on known variables. In regression models there is also the option of adjusting for a possible confounder.

In study I, II, and IV controls were matched for sex and birth year. Results in study III were adjusted for age, sex and family size, whereas in study V correlations were stratified by sex and zygosity. Results in study I, II, and IV were adjusted as well as stratified for IQ.

A mediator is not a confounder but an effect we often want to study. In study IV, we concluded that adjusting for IQ attenuated associations between bipolar disorder and officer suitability. This was interpreted as IQ partially mediating the effect of bipolar trait on officer suitability.

### 5.2.1.4 *Random errors*

Random errors are errors caused by chance. Most of the results presented in this thesis are based on large datasets, which reduces the risk of random errors. However, some sub-analyses were based on small populations, e.g., the comparison of half-siblings in study I.

### 5.2.2 *External validity*

External validity refers to the extent that results of a study can be generalized to other situations and persons. All studies included in this thesis are based on nationwide registers where data was collected for a long time period. It is therefore feasible that results are generalizable to other nationalities.

### 5.2.2.1 *Assumptions of the twin design*

Twin studies in general have been accused of inflating estimates of the genetic component, since they rest on the *equal environments assumption*. This assumption corresponds to the idea that MZ twin pairs and DZ twin pairs share equal environment, an assumption that has been challenged (Plomin, 2008; Visscher, Hill, & Wray, 2008). If MZ twins share more environment than DZ twins, this would lead to an overestimation of the genetic component. On the other hand, the equal environments assumption has been tested in several studies and seems to be reasonable stable for most traits investigated (Plomin, 2008).

### 5.2.3 *Content validity*

Content validity is a non-statistical type of validity that determines

whether a test covers a representative sample of the behavior domain to be measured (Anastasi & Urbina, 1997). We used creative professions as a test for creativity in study I, II, and V, a definition which is different from that of many previous investigations of the association between creativity and psychopathology. Previous studies often relied on third parties defining the creative output (e.g., being mentioned in Who's who, receiving reviews in the New York Times Book Review or through the judgment of experts (Karlsson, 1970; A. M. Ludwig, 1992; McKinnon, 1962)). This latter approach largely taps into eminent creativity (*big-C*), considered different from everyday creativity (*little-c*), which is more often addressed in creativity research. Our use of occupation as a proxy for creativity does not completely fit with either *big-C* or *little-c*. This problem was previously addressed by Kaufman et al., suggesting the term *pro-c* for 'individuals who are professional creators, but have not reached eminent status' (2009). These authors also argue that the addition of *pro-c* better represents the developmental trajectory of creativity in a person's life. They also point to the weakness of using expert opinion, considering the many examples in history of now obscure artists, inventors, and scientists that were once seen as the future of a field.

#### 5.2.4 Ethical consideration

The studies included in this thesis were approved by the Regional Ethics Committee at the Karolinska Institutet (2005/174-31/4; 2008/1735-31/3; 2009/939-31/5). Individuals included were identified through national registers. In order to safeguard the integrity of these individuals, national registration numbers were replaced with a unique identification code ensuring that no one could be identified in person.

While a benefit of the results presented in this thesis may be to de-stigmatize patients with psychiatric disorders, we have some concern that findings of an association between creativity and psychopathology may also lead to prejudices towards creative individuals and creativity in general. We have therefore strived to present our results as balanced as possible, and avoided to draw simple conclusions.

### 5.3 GENERAL DISCUSSION

The *Mad Genius* is a recurring stereotype of contemporary cultural expression. Given the impact of the idea, however, the empirical basis is comparatively scant. The main part of the literature concerning creativity and psychopathology consists not of original studies, but rather of opinions. Several studies reviewed in this thesis have also received serious criticism on methodological grounds (Schlesinger, 2009), e.g., retrospective designs, lack of control group and different ways of measuring creativity and psychopathology. Both creativity research and

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psychiatric nosology is characterized by a common challenge; the validity of the instruments and definitions, defining both creativity and psychiatric syndromes (Kendler, 1990; Runco, 2007). The main aim of this thesis is therefore to investigate creativity and psychopathology using large scale population based epidemiological methods. All studies included prospectively collected data and a control group. The psychiatric diagnoses used in study I – IV have been validated and our use of creative and executive professions has face validity. As has been discussed elsewhere results are generalizable (chapter 5.2.3).

Nevertheless, one might well raise concern over observational epidemiology in general. Many reported associations are spurious, and true associations are often exaggerated (Grimes & Schulz, 2012). These problems may have been inflated by the increased use of large data bases, as those used in the present thesis. Large cohorts add in precision, but not necessarily in validity. In 1965, Hill proposed a list of nine considerations to evaluate causality: strength of association, consistency of the observation, specificity of the relationship, temporal association, biologic gradient (dose-response effect), plausibility, coherence with other evidence, experiment, and analogy (1965). Similar guidelines have stressed *strength of associations* as important and suggested that weak associations, e.g., relative risks and odds ratios of less than 2, to be discounted (Grimes & Schulz, 2012). It is tempting to assume that strong associations are more probable to be causal than weak ones. Most associations between creativity and psychopathology demonstrated in this thesis are weak (study I and II). However, it is not certain that every component cause has a strong association with the outcome that it produces. In fact, it may also be that a strong association is noncausal, a confounded result stemming from another unknown risk factor. Rothman argues that ‘If weak associations can be causal and strong associations can be noncausal, it does not appear that strength of association can be considered a criterion for causality.’ (2012). Similar criticism can be raised regarding Hill’s other considerations. Rather than simple checklists, Rothman argues for a process based on *conjecture and refutation* echoing Karl Popper (2002). Study I and II of this thesis are generally supported by previous findings in smaller studies. Thus, the empirical basis is reasonable for creativity being associated with schizophrenia and bipolar disorder. Importantly, for schizophrenia, increased creativity is manifested in individuals with subsyndromal symptomatology and in the healthy relatives of patients, while for bipolar disorder studies affirm an association in both patients and relatives. Studies range from retrospective studies of eminent personalities, to smaller cohorts examined with established psychometric instruments, and on to nation-wide studies of creative occupations presented in this thesis (study I and II).

The diverse cognitive and neural underpinnings suggested for the association between creativity and psychopathology have been numerous. It is beyond the scope of this thesis to review these different ideas, but a recurring idea for *psychosis* has been its similarities with divergent thinking. For example, one study using positron emission tomography demonstrated a negative correlation between divergent thinking and dopamine receptor binding potential in the thalamus (de Manzano, Cervenka, Karabanov, Farde, & Ullen, 2010). Since the thalamus can be conceptualized as a central for information processing, the result of this alteration would be a reduction in filtering of information flow (*noise*) and a subsequent excitation of cortical regions through decreased inhibition of prefrontal neurons. This leads to a decrease in prefrontal signal-to-noise ratio, with prefrontal cortical regions more easily switching to a wider association range, i.e., an increase in divergent thinking. Conversely, this decreased signal-to-noise ratio should be disadvantageous in tasks that require high levels of selective attention, and lead to an increased risk of unwarranted signals from the thalamus overwhelming cortical neuro-transmission resulting in cognitive disorganization and psychosis.

Sass argues that patients with schizophrenia hold self-detachment and a lack of authenticity at the core of their phenomenology (Louis A. Sass, 1998). This lack of authenticity could stem from a lack in *common sense*, possibly reflecting the suggested neurophysiological findings above, and illustrated by patients with schizophrenia outperforming controls in logical deduction in conflict with common sense (Owen, Cutting, & David, 2007). By not disregarding possibilities otherwise considered irrelevant, this loss in common sense, could provide access to otherwise inaccessible associations thereby increasing both *flexibility* and *originality*, two major components of divergent thinking (James C. Kaufman & Sternberg, 2010). Sass' apt observation of the similarities in T.S Elliot's diagnose of the modern society as suffering from 'a dissociation of sensibility: a widening rift between thought and emotion, intellect and sensation, and a general failure to achieve unification of sensibility', and Kraepelin's definition of dementia praecox as a 'loss of inner unity of intellect, emotion, and volition' also offers an explanation for the impact that artists with *schizoid* tendencies, rather than a manic disposition, have had the *last century* (Louis A. Sass, 1998). Thus, the overrepresentation of artists with schizoid tendencies during the last century might be primarily due to modern society's failure to 'achieve unification of sensibility' possibly mirrored by our results of stronger associations to artistic occupations in schizophrenia rather than in bipolar disorder (study I), and a consequence of us using national registries of the twentieth century. Indeed, Jamison has given ample support for

a historic overrepresentation of bipolar disorder in artists during the romantic era (1996).

For bipolar disorder specifically, increased ability for divergent thinking may also be driven by hypomanic periods with ensuing augmented fluency (MacCabe et al., 2010; Runco, 2007), which is another important aspect of divergent thinking (Goodwin & Jamison, 2007). This assumption is supported by observed increased productivity in creative individuals during hypomania (K. R. Jamison, 1989).

An alternative way to frame the association between bipolar disorder, creativity and leadership qualities is in terms of the *Behaviour Activating System* (BAS), which is a construct in Gray's theory of personality (Gray, 1981). BAS compounds several facets important for leadership, e.g., focusing on reward and reward-related goals, and persistent efforts in reaching goals after preliminary success. It has been suggested that patients with bipolar disorder as well as those at risk to develop the disorder have an increased sensitivity of the BAS (Johnson, Edge, Holmes, & Carver, 2012). Prospective studies indicate that BAS sensitivity is related to the onset of bipolar spectrum disorder, the shift from cyclothymia to bipolar II disorder, the shift from bipolar II disorder to bipolar I disorder, and a more severe course of mania among those diagnosed with bipolar I disorder (Johnson, Edge, et al., 2012). Moreover, mania can be conceptualized as inadequately high BAS output in terms of motor activity, arousal, elation, and confidence (Depue & Iacono, 1989).

In line with the proposed increase of BAS sensitivity in bipolar disorder, people with bipolar disorder more often stress goal attainment (*wanting*) and see achievement as essential to self-worth (Lam, Wright, & Smith, 2004). They are willing to expend more effort in situations involving reward (Hayden et al., 2008), a tendency not demonstrated in tasks without rewards. Studies in responses to reward have failed to demonstrate any increase in the initial response (*liking*) in patients with bipolar disorder (Berridge, 2007; Farmer et al., 2006; Roiser et al., 2009). However, studies demonstrate that bipolar patients seem to experience positive affective responses, such as confidence and energy, to success for a *longer duration* than healthy controls (Farmer et al., 2006). This leads to an ability to mobilize further in response to goal progress (Fulford, Johnson, Llabre, & Carver, 2010). Essentially, people with bipolar traits seem to *want* more intensively than do others, continue to want even after attaining a reward, and consequently endorse highly ambitious life goals (Alloy et al., 2012; Carver & Johnson, 2009; Johnson, Carver, & Gotlib, 2012). Thus, they are best characterized as highly *motivated* rather than hedonic. This motivation to achieve has been linked to both creativity and leadership effectiveness (Feist, 1998; Judge, Bono, Ilies, & Gerhardt, 2002).

However, while this tendency might invoke premorbid accomplishment, as suggested by the increased BAS sensitivity, it may also be the very thing that contributes to a more severe course of mania over time. This was highlighted in study IV, where results revealed that the likelihood of holding executive professions was lower among persons suffering from bipolar disorder compared to controls, even though patients were those most often receiving superior leadership assessments. Also, while study II demonstrated that patients with bipolar disorder more often held creative professions than controls, they generally did so to a *lesser* degree than their healthy relatives. Patients with schizophrenia had a decreased likelihood of holding overall creative professions, while their relatives conversely demonstrated an overrepresentation in these professions compared to controls. The results of this thesis therefore suggest that traits associated with schizophrenia and bipolar disorder, may be beneficial for creativity, as well as for leadership with regards to bipolar disorder, but that the actual disorders are detrimental.

The secondary aim of this thesis is to elucidate if the association between creativity and psychopathology is mediated through genetic factors under positive selection. Study I compared half-siblings suggesting that identified associations was not due to environmental factors, thus pointing towards a genetic underpinning. Study V established an overall genetic component in creativity, operationalized both as creative professions and through CAQ, contingent on sex. These findings can be seen in light of previous studies, such as in Karlsson's studies of relatives to patients with schizophrenia indicating that certain branches of kindreds were high in both schizophrenia and giftedness, whereas others were low in both (1970).

Crucial to the study of creativity and psychopathology is if this association may explain the observation of high heritabilities (genetic component), decreased fecundity, and the paradoxical stable prevalence of severe psychiatric disorders? Study III of this thesis affirmed a clear reduction in fertility in most severe psychiatric disorders, i.e., schizophrenia, autism, anorexia nervosa, but did not suggest that the decreased fertility was compensated for by increased fertility in siblings of patients. Bipolar disorder was found to be under weaker negative selection, however, also in bipolar disorder there was no clear concomitant increased fertility in siblings of patients to balance the reduced fertility in the patients themselves.

It may be questioned if current fertility rates can be used to consider past evolutionary processes. This is important because the prevalence of a trait depends on the selection of previous generations rather than the current one. Some arguments for contemporary fecundity reflecting fecundity of past generations are suggested. First, changes

in fecundity may reflect a biological cause for reduced fertility, which is unrelated to culture or setting (e.g., reduced sperm count). Second, there is some evidence that low marriage rates mediate the effect of psychiatric disorders on fecundity (MacCabe et al., 2009). If this is the case, then modern developments in contraceptives and child mortality would not affect past fecundity. Third, the stigma associated with psychiatric disorders in traditional communities is high, suggesting that the effects are not culture bound (Ng, 1997; Shibre et al., 2001).

Thus, results would seem to way against balancing selection in favor of mutation selection balance. However, it has been argued that reduced fertility in patients with severe psychiatric disorders and their relatives does not constitute evidence against positive selection on susceptibility genes for these psychiatric disorders (M. Del Giudice, 2010), but rather that the fecundity of all those holding the trait associated with increased risk of the disorder, e.g., increased creativity, should be taken into account first. Presently, there is no study that specifically has investigated fecundity in creativity, albeit one study having linked professional activity in poetry and visual art to mating success (Nettle & Clegg, 2006). In any case present results clearly demonstrate that there is no current positive selection for the investigated psychiatric disorders *per se*.

### 5.3.1 Final remarks

This thesis is the product of an often reiterated idea among clinicians in psychiatry, that some individuals suffering psychiatric disorder also demonstrate amazing achievements (Becker, 1978). One of the first patients I had the opportunity to meet in this context was suffering from bipolar disorder.

He was in a terrible state stricken by melancholic depression. His whole person revealed a complete drain of energy, and I then had great difficulties to imagine that he was in fact a great entrepreneur. On our second visit together with his wife, I was told that just some months earlier he had celebrated his fiftieth birthday. This occasion took place in the summer on an island in the Swedish archipelago with hundreds of guests participating. In his usual abundance of energy, his wife said, he had been able to convince a Swedish fighter pilot to fly over the island in a show much appreciated by the people below. As we sat in my small room at the hospital, there was winter and snow falling outside the window, I looked at him and realized that *this* was bipolar disorder.

Psychiatry has come a long way since Hippocrates, Kraepelin and even since Robert Spitzer (Shorter, 1997). While the results of this thesis lack a direct implication for clinical practice, I hope that they may be seen in light of a psychiatric practice that stresses the need for a firm scientific basis, but also allows for an individual perspective. The

latter can be achieved by using new technologies, through the renewed interest in studies of psychiatric phenomenology, as well as from clinicians interacting more with each patient. Evidence based medicine is defined as ‘the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of *individual* patients’ (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996). Thus, it is vital to incorporate results from large clinical trials with individual information gathered by the clinician for the benefit of the patient. The future harbors great possibilities for psychiatry. I am excited to be a part of that development.



## 6 Conclusion

IN CONCLUSION, THIS thesis provides support for a familial cosegregation of both schizophrenia and bipolar disorder with creativity, while suggesting that this may be mediated through a genetic mechanism. Results do not, however, support that any psychiatric disorder *per se* is under positive selection.

The association of certain psychiatric disorders with creativity highlights the need for an individualized treatment approach combining results from large clinical trials with individual patient information.

## 7 Svensk sammanfattning

DET GALNA GENIET är en återkommande stereotyp i samtida kultur. Men med början i Lombrosos bok om genialitet och galenskap publicerad 1888, så har det kommit ett ökande antal empiriska studier de senaste decennierna som tyder på att det verkligen finns ett samband mellan kreativitet och psykopatologi. Trots det är det empiriska underlaget fortfarande bristfälligt, då tidigare studier ofta vilar på biografiska data och små material. Det primära syftet med denna avhandling är därför att undersöka frågan om ett samband mellan kreativitet och psykopatologi genom att använda epidemiologiska metoder på populationsnivå.

Det föreslagna sambandet mellan kreativitet och psykopatologi har ofta tolkats ur ett evolutionärt perspektiv där bördan av psykisk sjukdom skulle kompenseras av fördelarna med ökad kreativitet. Det sekundära syftet med denna avhandling är därför att belysa om en förmodad koppling mellan kreativitet och psykopatologi kan medieras genom genetiska faktorer under positivt urval.

I vår första studie (studie I), som bygger på Svenska nationella register, undersökte vi sannolikheten för att inneha ett kreativt yrke (konstnärliga och vetenskapliga yrken) bland individer ( $n \sim 300\ 000$ ) med schizofreni, bipolär sjukdom eller unipolär depression samt bland deras friska släktingar jämfört med friska kontroller. Resultaten visade att personer med bipolär sjukdom och friska syskon till personer med schizofreni eller bipolär sjukdom är överrepresenterade i kreativa yrken. Vi följde upp dessa iakttagelser i studie II bland ett betydligt större antal patienter ( $n \sim 1\ 200\ 000$ ) för att kartlägga andra psykiatriska diagnoser och för att validera tidigare resultat.

Studie IV undersökte en idé i nära anknytning till den om kreativitet och psykopatologi: att bipolär sjukdom är vanligt förekommande bland framstående ledare, t ex Winston Churchill, Abraham Lincoln och Napoleon Bonaparte. Resultaten visade att personer med bipolär sjukdom utan samsjuklighet och deras friska syskon var överrepresenterade i det högsta skiktet av officerslämplighet, en skattning av ledarpotential. Syskonen var också överrepresenterade i chefsyrken, speciellt i subgruppen med politiska yrken.

I studie III närmade vi oss det evolutionära perspektivet genom att undersöka fertiliteten hos personer med psykiatriska syndrom och deras friska syskon. Totalt  $\sim 2,3$  miljoner personer inkluderades. Med undantag för kvinnor med depression, så hade personer med psykiatriska diagnoser betydligt färre barn än befolkningen i stort.

Det evolutionära sammanhanget undersöktes vidare i studie V, där vi systematiskt gick igenom litteraturen avseende genetik för kreativitet och dessutom uppskattade ärftlighet av kreativitet i två nya originalstudier. Resultaten stödjer en genetisk komponent för kreativitet, och för första gången tyder data på att denna är beroende av kön.

## SVENSK SAMMANFATTNING

Sammanfattningsvis ger avhandlingen stöd för ett familjärt samband mellan både schizofreni och bipolär sjukdom med kreativitet. Resultaten talar för att sambandet skulle kunna ha en genetisk grund. Däremot finns inget stöd för att någon psykiatrisk sjukdom i sig skulle stå under positivt urval.

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