Autism's anatomy

Verhoeff, Berend

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> One cannot speak of anything at any time; it is not easy to say something new; it is not enough for us to open our eyes, to pay attention, or to be aware, for new objects suddenly light up and emerge out of the ground. (Foucault, 1972: 44f)

> It is also inadequate to define syphilis phenomenologically rather than conceptually, in the manner that animals and plants might be defined on the basis of their characteristics. For it is naïve to think that, although its historical development has been tortuous and complicated, we can today arrive at the concept of the disease entity "syphilis" simply and safely merely by using current techniques of observation and experiment. (Fleck, 1935/1979: 21)

Abstract

Using the conceptual tools of philosopher of science Ludwik Fleck, I argue that the reframing of autism as a neurodevelopmental spectrum disorder is constrained by two governing 'styles of thought' of contemporary psychiatry. The first is the historically conditioned 'readiness for directed perception' of, and thinking in terms of, ontologically distinct diseases. The clinical gaze of mental health professionals, the bureaucratic needs of health administration, the clinical and scientific utility of disease categories, and the practices of autism-oriented advocacy groups all imply a bias toward thinking about autism and related disorders as ontologically distinct psychiatric and scientific entities. Second, within the 'neuromolecular style of thought', mental disorders are more and more located at the neurobiological levels of the brain. In autism research, one of the biggest challenges is the identification of autism's neurobiological

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singularity. However, at a moment when biological and categorical approaches toward autism face serious empirical difficulties, a balance is established that holds together these two styles of thought. With a need to account for some of the most persistent uncertainties and conflicts in autism research, namely ubiquitous heterogeneity and a failure to identify disease specific biomarkers, the reframing of autism as a neurodevelopmental spectrum disorder satisfies the scientific, institutional and socio-political needs for stability and homogenization.

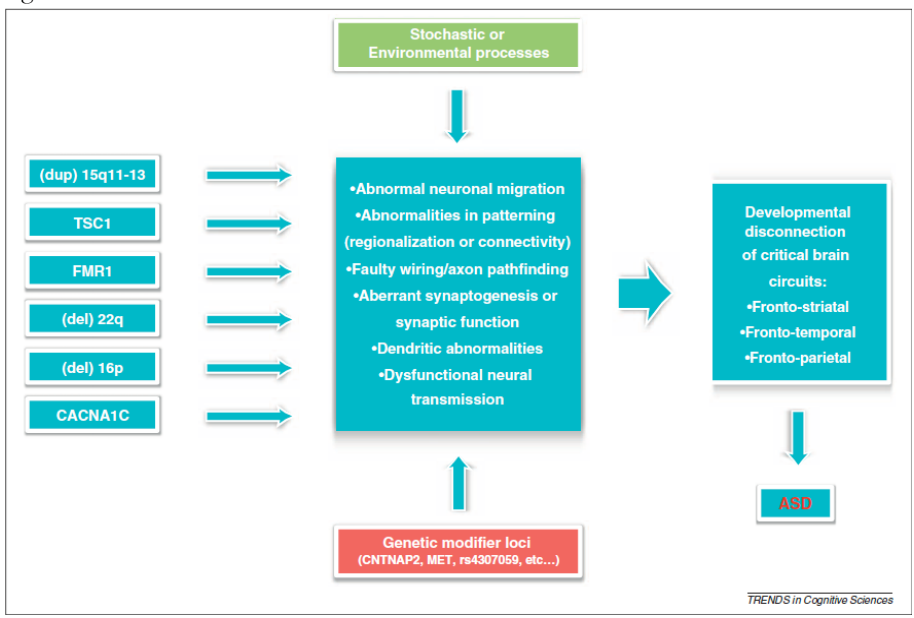
Introduction

Today, autism is understood to be both a 'spectrum' disorder and a 'neurodevelopmental' disease of the brain – at least by leading autism experts and those who are responsible for organizing the criteria and categories of autism and related disorders in the latest version of the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-5*). According to one of the members of the *DSM-5* Neurodevelopmental Disorders Work Group, 'the term *autism spectrum disorder* … reflects current widespread consensus that autism is best considered as existing on a spectrum with variable manifestations across life span, gender, and intellectual level and/or language ability' (Happé, 2011: 540). In *A Parent's Guide to Autism Spectrum Disorder* (ASD), the American National Institute of Mental Health (NIMH) summarizes that 'the term "spectrum" refers to the wide range of symptoms, skills, and levels of impairment, or disability, that children with ASD can have' (NIMH, 2011: 1). In moving from representing autism as a single disorder to autism as a spectrum disorder, the biological and hereditary nature of autism remains unchallenged. However, the earlier search for a discrete 'autism-gene' (Bonora et al., 2003) or a distinct deficit in a tentative cognitive module (Baron-Cohen et al., 1985) nowadays appears naïve. In line with the spectrum approach, more complex images of the etiology and pathophysiology of autism have replaced 'simple' essentialist notions of autism.

Besides a spectrum disorder, autism has become a *neurodevelopmental* disorder in which multiple deficits in the growth and development of the brain are assumed to underlie the diversity of abnormalities in social interaction and mental flexibility. Genes still play a role, but no longer as central determining factors. Several dozen or maybe even a hundred susceptibility genes are thought

to be involved – via the different molecules they express and in interaction with each other and environmental processes – in the disturbance of larger biological networks and pathways responsible for neuronal motility, axon guidance and the regulation and formation of synapses (see, for example, Voineagu et al., 2011). As Geschwind (2011) explicitly illustrates in a working model (see Figure 1), deficits in neurodevelopment and the neuroscientist's laboratory have become 'obligatory passage points' (Callon, 1986) for producing truths about autism.

Figure 1.



This model illustrates how autism risk alleles, such as those shown at the left, and environmental factors act on systems of neurodevelopment and lead to autism. Geschwind (2011: 413) argues that although gene expression and proteomic molecular studies identify molecular and biological pathways that provide a source of convergence, 'the ultimate convergence must lie in neural systems'. At this neurodevelopmental level, 'the convergent process will likely be disconnection of the circuits outlined in the far right box because these systems are thought to underlie the core deficits of ASD'. Adapted with permission from Geschwind (2011).

However, while medical and scientific authorities emphasize that autism is a neurodevelopmental spectrum disorder, other kinds of experts in the social sciences analyze autism – its emergence, treatments, theories, institutions and conceptual transformations – from a social, cultural and historical perspective (for example, Eyal et al., 2010; Silverman, 2011). Most social studies of autism do not deny the seriousness or biological basis of the conditions that are labeled as autism (see, for example, Nadesan, 2005; Grinker, 2007; Eyal et al., 2010), but focus primarily on socio-cultural, economic and political factors that are involved, for instance, in the recognition, spread, interpretation and remediation of autism. Eyal et al. (2010), for example, acknowledge that autism is usually explained in biological terms, but – in their analysis of the 'autism epidemic' – they focus mainly on social factors and cultural changes in medical practice such as the reorganization of expertise, processes of deinstitutionalization of mental retardation, parental activism and an increase in the availability of services. Like most other social autism studies (for example, Nadesan, 2005; Grinker, 2007), Eyal et al.'s study does not integrate specific scientific practices and theoretical content into (social) explanations and understandings of conceptual transformations of the scientific object of autism and, according to Fitzgerald (2012: 52), 'the authors situate their account exactly on the fault-line of biological and cultural explanation'.[36]

In these social histories of autism, cultural change and scientific explanations are generally approached separately, and the specific ways in which scientific practices and developments are socially and historically situated and intermingle with social and institutional developments remain rather unanalyzed. This is not the place to discuss whether this is a significant limitation of these particular histories of autism. However, as this chapter argues, in order to understand certain aspects of the recent history of autism – in particular, the rise of a new view of autism as a 'neurodevelopmental spectrum disorder' – one needs to combine attention to developments, aims, challenges and failures of contemporary biomedical autism research with an

[36] In a series of interviews with autism neuroscientists, Fitzgerald (2012) is particularly intent on taking autism neuroscience seriously. However, as he acknowledges, his 'unglamorous empirical sociology' stays at the level of 'neuroscientists *own* accounts of their daily assumptions and practices' and does not try to explain changes in the conceptualization of autism (p. 210, emphasis in original).

investigation of the historical and cultural matrices in which autism as a medical category emerged and currently circulates.[37]

Drawing upon the work of Ludwik Fleck (1935/1979) – who is viewed today as a pioneer of the historical and sociological approach to the production of scientific knowledge (Fagan, 2009; Hedfors, 2007; Löwy, 2004a) – and drawing upon contemporary studies inspired by Fleck (for example, Löwy, 2004a; 2004b; Rose and Abi-Rached, 2013; Rosenberg, 2003), I will propose a theoretical framework for an integrated account of the current views of autism. Fleck's notions of thought styles, thought collectives and passive and active elements of knowledge are especially well adapted to describing 'medical facts' (such as those of contemporary autism research) that is 'entities that are developed and stabilized through multilevel interactions and circulation in heterogeneous networks, that are dynamic and historical, and that are at the same time strongly material and cultural' (Löwy, 2004a: 443). Using Fleck's conceptual tools, this chapter aims to understand the rise of a neurodevelopmental spectrum disorder in a way that neither ignores the 'hard residue of material reality' (or 'passive elements of knowledge'), nor ignores the importance of historical, social and institutional ('active') elements of and constraints on thinking about autism (Fleck, 1979).

The third section of this chapter, which follows this introduction and some general remarks, briefly discusses the central concepts introduced by Fleck. Instead of providing a neat way to disentangle scientific from cultural aspects of current understandings of autism, Fleck's conceptual tools enable the development of a cohesive account of the rise of a neurodevelopmental autism spectrum disorder. In this account the modified concept of autism becomes a solution for particular persistent uncertainties and conflicts in contemporary

[37] An interest in the material practices of biomedicine and medical cultures is certainly not new for historians or anthropologists of medicine and, according to Löwy (2011), is at least thirty years old. On the 'practice turn' in the history of medicine, see also Pickstone (2011). Löwy (2011: 122) furthermore points out that this 'practice turn' in the history of medicine and the adoption of methods of inquiry of historians and sociologists of science and technology came at a cost, namely a neglect of an earlier generation of historians of medicine. In general, she argues, 'we know much more about biomedical "laboratory life" than about the life of the clinics' and in a plea for 'more medicine into biomedicine studies', she suggests involving theoretical insights of scholars from earlier generations, such as Fleck, Temkin, Canguilhem and Foucault. Using the theoretical insights of Fleck, I hope this contemporary history of autism heeds Löwy's call for more medicine into (the history of) biomedicine.

autism research, namely ubiquitous heterogeneity and a failure to identify specific biomarkers for autism. This solution, I argue, which involves a reworking of the very object of explanation, must be understood as closely bound to and resulting from two organizing and constraining 'styles of thought' of contemporary Western psychiatry. The first 'style of thought,' which will be discussed in the fourth section, is the self-evident way of medical thinking in terms of ontologically distinct disease entities. This style of thought plays an important role in connecting, integrating and facilitating scientific, diagnostic, therapeutic, and bureaucratic practices. Something similar to what others have called the biological or 'neuromolecular' style of thought (Rose and Abi-Rached, 2013) will be discussed in the fifth section as a second central aspect of contemporary Western psychiatry. Before all that, I want to make some general remarks.

Why autism?

The recent shift in representing, classifying, studying and treating autism as a neurodevelopmental spectrum disorder should not be imagined as an autism-specific, unique or isolated phenomenon. Similar new ways of investigating, conceptualizing and categorizing psychiatric conditions in terms of neurodevelopment and spectra have been progressively emerging over the last decade. An increase in the number of scientific articles about the psychosis spectrum, the bipolar spectrum, the obsessive-compulsive disorder spectrum (see, for example, Ruhrmann et al., 2010), and new models that describe ADHD, depression, anxiety and schizophrenia (see, for example, Lewis and Levitt, 2002) as neurodevelopmental disorders indicate a broader transformation in thinking about psychiatric disorders.[38]

[38] In addition, the spectrum concept is certainly not new in psychiatry. Kety et al. (1968), for instance, used the spectrum metaphor to introduce a 'schizophrenia spectrum of disorders' that linked patients diagnosed with schizophrenia with 'uncertain schizophrenia' and 'inadequete personality' observed in biological relatives. Even earlier, Kretschmer (1921) proposed dimensional models for schizophrenia (schizothymic, schizoid, schizophrenic) and for affective disorders (cyclothymic temperament, cycloid psychopathy, manic-depressive disorder) to emphasize a hypothetical common pathophysiology. Furthermore, levels of severity (mild, moderate,

However, autism does make a special case that is worth exploring in detail. As the first DSM category with the word 'spectrum' in its name (APA, 2013) and the most researched and funded neurodevelopmental disorder (Bishop, 2010), autism is an important forerunner in this broader shift and can serve as a paradigm case for understanding recent developments in psychiatry.[39] As we will see, psychiatry is on the one hand fragmented and mainly organized around specific disease categories, but on the other hand, there are general tendencies or 'styles of thought' in psychiatry and medicine that transcend the level of individual disease categories. A focus on autism reveals and demonstrates the dynamics between these more abstract levels of general psychiatric thought and the concrete level of disease specific research and practice. Although these dynamics and conceptual developments are not specific for autism, thinking in terms of a spectrum is most accepted and stabilized – compared to other mental disorders – in both professional and lay perceptions of autism. In addition, autism's highly developed neuroscientific research makes it possible to explore with autism how general psychiatric and medical styles of thought are reflected in cutting-edge psychiatric research, and how, in turn, specific developments within the advanced field of autism affect psychiatry at large.

Furthermore, despite a general tendency in medicine towards 'personalized medicine' (see Hamburg and Collins, 2010), a persistent use of broad categories like obesity and coronary heart disease (see, for example, Jones, 2013), which gather heterogeneous phenomena, could be seen as comparable to the recent spectrum approach in psychiatry. These broad disease categories have their own historical, material, professional and organizational constraints and, comparable to the spectrum categories in psychiatry, they also function as intermediaries between several communities of practice in order to maintain a shared identity across sites (Bowker and Star, 1999).[40] Yet, in contrast with the

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severe) could already be specified for several disorders (for instance, depression and intellectual disability) in all earlier DSM editions.

[39] There have also been earlier dimensional and spectrum concepts related to autism (for example, Rutter, 1968; Wing and Gould, 1979; Wing, 1996). How they are both similar to and importantly different from more recent thinking in terms of the 'autism spectrum' will be discussed in more detail in part 6, 'Rise of a neurodevelopmental spectrum disorder'.

[40] Bowker and Star would call these categories 'boundary objects,' as they 'inhabit several communities of practice and satisfy the informational requirements of each of them.... Such objects have different meanings in different social worlds but their

spectrum categories, the unity of these broad and heterogeneous categories is somewhat less puzzling and found in 'straightforward' phenotypes (a Body Mass Index of more than 30 kg/m^2 in obesity, or blood pressure above 100-140 mmHg in hypertension) or in a particular organ that is affected (heart coronaries in coronary heart disease). Whereas, the meaning of a 'spectrum' in psychiatry and what it is that keeps a spectrum category together is very ambiguous. As we will see, unlike the broad categories in general medicine and besides being intermediaries between several communities, an important and specific function of the idea of an autism *spectrum* is legitimizing and stabilizing the continuous search for autism's neurobiological foundation and to hold the heterogeneous (and fuzzy) category of autism together as a valid, researchable, clinically useful and convincing diagnostic entity.

Moreover, this Fleckian approach to autism should not be read as a critical attack or *normative* evaluation of the neurodevelopmental spectrum idea of autism, or of the autism research field in general. Nor is it a proposal for an alternative model to conceptualize and investigate autism. Instead, it aims to understand the recent history of autism in a novel way that combines cutting-edge scientific developments with social, historical and institutional determinants and constraints in a cohesive account. Nevertheless, in revealing a particular way in which 'biomedical facts' about autism and the very idea of autism itself came into being and developed, this analysis does open up space for thinking about the intersections between 'the clinic,' 'the lab,' and society and how they might be connected in future autism research and clinical practice.

Ludwik Fleck

In his pioneering study, *The Genesis and Development of a Scientific Fact* (1935/1979), Fleck offers an account of scientific facts not as things to be discovered or revealed, but as products of scientific practices, technologies and historically and socially preconditioned ways of seeing and thinking. Fleck's epistemology concerned the acquisition of scientific knowledge, and his history of syphilis and the Wasserman reaction illustrates the dense social, material and

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structure is common enough to more than one world to make them recognizable, a means of translation' (Bowker and Star, 1999: 297).

cognitive network in which scientific knowledge arises, stabilizes and changes. According to Fleck, science and its products are fundamentally rooted in a specific and unique history. Within a particular scientific field or 'thought collective' – defined by Fleck as 'a community of persons mutually exchanging ideas or maintaining intellectual interaction' (ibid.: 39) – tradition, education, and familiarity produce a '*readiness for stylized (that is, directed and restricted) perception and action*' (ibid.: 84).

This readiness for directed perception, for which being educated and experienced within a particular scientific field is epistemologically fundamental, is 'the main constituent of [a] thought style' (ibid.: 92). Fleck illustrates how the production of scientific knowledge is determined by and can only arise in a context of collectively structured background knowledge. Ways of making observations, shaping and establishing the very object of explanation, defining the set of problems, and using specific methods, techniques and languages are all constrained and appear inevitable within a particular style of thought. Furthermore, besides historical and socio-cogitative constraints on scientific thought, an additional source of 'resistance' to 'the free unfolding of ideas' (Fleck, 1979: 84) arises due to intrinsic properties of the material world:

> [T]here are always other connections which are also to be found in the content of knowledge that are not explicable in terms either of psychology (both individual and collective) or of history. For this very reason these seem to be "real," "objective," and "true" relations. We call them the passive connections in contrast with the others which we call active. In our history of syphilis the combination of all venereal diseases under the generic concept of carnal scourge was thus an active association of the phenomena, explained in terms of cultural history. In contrast, a restriction of the curative effect of mercury … that "sometimes mercury does not cure the carnal scourge but makes it even worse" represents a passive association with respect to the act of cognition. (Fleck, 1979: 10)

Obviously, Fleck's example of a passive connection can only be formulated using the concept of carnal scourge that contains passive as well as active elements. Fleck recognizes that the 'passive resistance' of material elements of the natural world and the 'active resistance' of scientific thought created by

historical, social and psychological connections 'cannot be separated from each other completely either logically or historically' (ibid.: 95). Furthermore, 'the more developed and detailed a branch of knowledge becomes, the smaller are the differences of opinion' (ibid.: 83) and the greater the number of active and passive connections will be. As a result, a dense network of active and passive connections that constitutes a particular style of thought seems to achieve a kind of inevitable stability, in which conventionalism is considerably restricted and the active elements – 'as a result of education and training as well as through [the scientists] participation in the communication of thoughts within his collective' (ibid.: 141) – become invisible. At this point, a 'tendency to reify and objectivize the conceptual creations of scientific thought arises' (ibid.: 144), and a 'resistance to anything that contradicts [the closed system of knowledge]' helps to guard a kind of 'harmony of illusions' (ibid.: 27).

However, change in style of thought, that is change in readiness for directed perception, can be generated by communicative interactions within and between thought-collectives: 'communication never occurs without a transformation, and indeed always involves a stylized remodeling, which intracollectively achieves corroboration and which intercollectively yields fundamental alteration' (ibid.: 111). According to Fleck, thought collectives have an internal interactive structure made up of an 'esoteric' circle of experts and specialists, and an exoteric circle of 'educated amateurs'. Once scientific facts are stabilized within the inner 'esoteric' circle of a particular thought collective, they often move outside and encounter 'other scientific communities, but also other social groups: users of science, practitioners, politicians, the public at large. This is a bi-directional process. Proto-concepts originating in society at large, such as 'syphilic blood', affect the development of scientific facts, while such facts in turn influence society and culture' (Löwy, 2004b: 513).

Fleck's approach makes it possible to analyze the reframing of autism as a 'neurodevelopmental spectrum disorder' as a complex dynamic phenomenon rooted in multilevel interactions between 'passive elements' – such as the structure of neural pathways and the heterogeneity of biomarkers – and 'active elements', like the cultural history of psychiatry as a medical profession or historical modes of classifying mental disorder.

Distinct disease pictures: the contemporary style of medical thought

Within medicine and the medical sciences, Fleck (1927/1986) argued,

> [A]bnormal morbid phenomena are grouped round certain types, producing laws of a higher order, because they are more beautiful and more general than the normal phenomena which suddenly become profoundly intelligible. These types, these ideal, fictitious pictures, known as morbid units, round which both the individual and the variable morbid phenomena are grouped, without, however, ever corresponding completely to them – are produced by the medical way of thinking, on the one hand by specific, far-reaching abstraction, by rejection of some observed data, and on the other hand, by the specific construction of hypotheses, i.e. by guessing of non-observed relations. (Fleck, 1927/1986: 40)

With the assumption that the development of science is only a matter of time, technical possibilities and accident, Fleck continues, we would never be able to grasp 'why a phenomenon which is accessible to everybody had been observed at the given moment for the first time, and even almost simultaneously by several researchers' (ibid.: 41). For instance, despite the repeatedly emphasized recognizability and distinctiveness of autism (see, for example, Frith, 1989; Kanner, 1965; Volkmar, 1998), the clinical unit of autism emerged markedly recent (in 1943). Yet, many pre-Kannerian historical figures, eccentric geniuses and religious figures, such as Newton and Michelangelo, have been retrospectively diagnosed as cases of autism or Asperger's disorder (Fitzgerald, 2005).

Furthermore, Hans Asperger – separated from Leo Kanner by an ocean and a war – introduced his 'autistic psychopathy' only one year after Leo Kanner introduced his fairly similar 'early infantile autism' (Asperger, 1944).[41] For Hacking (2006), this was certainly not a coincidence as Asperger and Kanner,

[41] I will not go into detail about the particular cultural, social and political conditions that made the specific emergence of autism possible (see, for instance, Nadesan, 2005), but the term 'autism' was coined by Swiss psychiatrist Eugen Bleuler around 1910 as one of the symptoms of schizophrenia. By the time Kanner introduced his new diagnostic entity, autism was a term with wide use in German psychiatry (see Evans, 2013; Nadesan, 2005; Verhoeff, 2013/Chapter 3).

although they never met nor corresponded, came from the same medical culture – the same 'esoteric circle'.[42] Without the idea that distinct scientific periods possess specific styles of thinking, the rise and development of certain definite clinical units would become unintelligible. However, thinking in terms of ontologically distinct diseases is 'by no means the only logical possibility. As history shows, it is feasible to introduce completely different classifications of disease' (Fleck 1979: 21).

From idiosyncrasies to distinct disease entities

The insightful work of historian of medicine Charles Rosenberg reveals some of these 'completely different classifications of disease'. He illustrates that the perception that corporeal or psychological pain and suffering can and should be thought of as specific disease entities existing outside their unique appearances in particular individuals did not become pervasive until the late nineteenth century (Rosenberg, 2006).[43] Before this period, disease was not imagined as a set of different entities, each with specific signs and symptoms, and a specific etiology, course and pathophysiology. Instead, disease was a variable physiological state of the individual patient that resulted from 'a cumulative interaction between constitutional endowment and environmental circumstances' (Rosenberg, 1977: 487). Owsei Temkin, an earlier important historian of medicine, called this the 'physiological' understanding of disease, distinct from the later 'ontological' understanding of diseases as existing

[42] Hacking analyzes the development of human categories like multiple personality disorder (Hacking, 1995), obesity and also autism (Hacking, 2007) from a particular perspective. With his term 'interactive kinds' he attends to the way in which people react to being classified and described, and how, as a result of these reactions, the very people and the classifications that are supposed to cover them go through a process of alteration. Eyal et al. (2010) use Hacking's feedback loop to explain the rise in people diagnosed with autism. In these accounts, the contribution of particular scientific content and styles of thought to the development of human categories remains largely unanalyzed.

[43] This does not imply that there are no earlier examples of hypothetical disease entities. Even psychological ailments had been viewed as conditions such as melancholy or hysteria and 'humeral explanations of temperamental peculiarity are as old as Western medicine itself' (Rosenberg, 2006: 412). However, the disease concepts they brought into play were fundamentally different from those that became habitual by the end of the nineteenth century. See Thomas Sydenham's *Epistolary Dissertation on the Hysterical Affections* of 1682 as an earlier attempt at classifying forms of madness.

independently of their unique appearances in particular individuals (Temkin, 1977).

In the former period, the body, health and disease were understood in holistic terms of equilibrium, physiological adjustment and vital powers, in which food, water, air, climate, living conditions and even morals played a necessary and irreducible role. Disease was understood in individual rather than general terms and 'health was a consequence of a symbiotic relationship between nature, society and the individual' (Grob, 1998: 192).[44] Clinical treatment and physicians' importance was largely independent of any nosological system and involved the ability to recognize and deal with the multitude of environmental circumstances and the idiosyncrasies of each patient.[45]

This perception of disease gradually changed around 1870 with a new emphasis on diseases as discrete entities with specific underlying mechanisms. Earlier nineteenth century postmortem pathology, the clinical use of 'instruments of precision' such as the thermometer, blood and urine chemistry and microscopy, and the growing status of what we now call the biomedical sciences (histology, physiology, biochemistry) all contributed to this new ontological way of thinking about disease. A lesion-based notion of disease, and later germ theories of infectious disease in combination with new forms of knowledge arising from bacteriology and laboratories of biochemists and physiologists, reinforced the idea that diseases could be delineated in precise and measurable terms. In addition, and of particular importance for psychiatry, 'the late-19th-century vogue for heredity and evolution constituted another significant factor, linking biology and behavior, mind and body, past and present … Like germ theory, heredity provided … a reassuringly somatic mechanism with which to explain a variety of unsettling emotions and problematic behaviors' (Rosenberg, 2006: 413). Alcoholism, neurasthenia, hypochondria, anorexia, homosexuality and kleptomania all emerged as distinct

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[44] Even something as widespread and terrifying as the yellow fever epidemic of 1793 in Philadelphia 'could be construed as the consequence of a peculiarly tainted microenvironment – presumably something in the atmosphere – coupled with an individual idiosyncrasy, which explained why some succumbed, some recovered, and others never fell ill during a local outbreak' (Rosenberg, 2007: 3).

[45] The regulation of secretions – by extracting blood or promoting urination, defecation or perspiration – in order to recover a damaged equilibrium, was the physician's most powerful therapy.

diseases by the end of the nineteenth century, and heredity seemed a determining factor, rather than one of the many interacting individual and environmental factors that determined health and disease in earlier times.[46]

Autism as a distinct disease

Part of this new style of medical thought was Emil Kraepelin's very influential system of classification of psychiatric disorders, published in the 6th edition of the *Lehrbuch der Psychiatrie* (1899). Kraepelin, often regarded as the founder of modern psychiatry, introduced 16 categories based on patterns of symptoms with each containing a particular 'essence' and (in theory) specific biological disturbances (Berrios and Hauser, 1988).[47] There is, however, no clear historical path from Kraepelin's biomedical model of nosological entities to the contemporary 'neo-Kraepelinian' era of biological psychiatry and DSM-based education, clinical practice and research. Throughout the twentieth century, the ontological understanding of disease had not been as steady and monolithic in psychiatry as it was in the rest of medicine. For instance, Adolf Meyer's 'mental reaction-types' and his holistic 'psychobiological' understanding of human behavior (Meyer, 1908), Freudian psychoanalytical theories, and Karl Menninger's emphasis on interpersonal, social, and environmental factors in personal maladjustment (Menninger, 1963) were all very influential perspectives that were not based on disease entities and explicitly opposed the Kraepelinian nosology of distinct diseases of organic or hereditary origin.

Even though holistic and psychodynamic approaches were never completely hegemonic – for much of the twentieth century, American psychiatry was a divided and ambivalent specialty (Grob, 1998) – nosological systems were of minor importance in American psychiatry until the late 1970s. Closer to an individual understanding of disease and in the spirit of Meyer's 'genetic-dynamic' framework, which 'shaped several generations of American psychiatrists,' (ibid.: 202) American psychiatrists were generally more 'interested

[46] Social and political aspects such as managing deviance and rationalizing health policies and the relation with this idea of distinct disease entities are not discussed here, but these aspects undoubtedly played a role in the emergence of this new medical way of thinking. I will pay some attention to this in discussing autism in relation to regulatory practices.

[47] There is, of course, much more that can be said about the emergence of academic psychiatry in the late nineteenth century. See, for example, Berrios and Porter (1995) and Berrios (1996).

in the person and his life experiences rather than, like so many of our continental colleagues, primarily in a disease process' (Lidz, 1966: 321).

Remarkably, it was within this Meyerian and psychodynamic, anti-Kraepelinian psychiatric culture that Leo Kanner, who was appointed by and worked together with Meyer himself at the Johns Hopkins Hospital in Baltimore (Neumärker, 2003), proposed the distinct diagnostic entity of 'early infantile autism' on the basis of descriptions of the behavior of 11 children with similar symptoms. Very much against the established psychoanalytic style of thinking and theorizing about psychological problems in children in terms of unconscious thought processes, libidinal instincts and destructive impulses and fantasies (Evans, 2013), Kanner's descriptive approach in child psychiatry was clearly Kraepelinian. He presented autism as 'a "unique syndrome," not heretofore reported' (Kanner, 1943: 242) and he hypothesized that children with autism came 'into the world with innate inability to form the usual, biologically provided affective contact with people, just as other children come into the world with innate physical or intellectual handicaps' (ibid.: 250).

The fact that Kanner had been educated in Berlin within the intellectual and institutional milieu of German medicine (Neumärker, 2003)[48] and that he was very well aware of Kraepelin's work and nosological system, might have played a role in his apparently anachronistic perception and introduction of a new disease entity. A few years after this introduction, he confidently argued that 'now that early infantile autism has a well-defined symptomatology and the syndrome as such can be recognized with relative ease, it is ready to apply for a place in the existing psychiatric nosology' (Kanner, 1949: 416). With an explicit reference to Kraepelin's scientific psychiatry, the major challenge for his distinct syndrome became 'to find a common denominator' and to identify 'the intrinsic nature of the condition as related or unrelated to the intrinsic nature of other conditions' (ibid.: 416-417). However, at least until the 1960s, many professionals in the field of child psychology and psychiatry were not quite ready to adopt this 'new' style of medical thinking about autism as a distinct disease entity. Instead of delineating syndromes and discovering the underlying nature of distinct diseases, they continued to employ psychodynamic terms such as 'autoerotism, primary narcissism and symbolic thinking to understand

[48] In search of better professional opportunities, Kanner moved to the USA in 1924 when he was 29 years old (Neumärker, 2003).

infantile psychopathology and problems with developing relationships' (Evans, 2013: 10).

Autism slowly started to settle as a recognizable syndrome in the 1960s and 1970s. A growing need for epidemiological studies and new experimental and neuropsychological tests required reliable behavioral descriptions (ibid.). Kanner's earlier descriptions became the central point of reference for further empirical studies (see, for example, Lotter, 1966). The term autism was less and less used to refer to the (psychoanalytically interpreted) symptom of disturbance in engagement with external reality, and instead came to stand for the entire syndrome that Kanner delineated. Again in line with the Kraepelinian tradition and Kanner's initial project, autism research became mainly directed at unraveling the 'intrinsic nature' and 'primary defects' of the disorder (Rutter, 1968). The arrival of *DSM-III* (APA, 1980) marked a definite neo-Kraepelinian turn, and autism was included as a distinct category in the new and soon prevailing nosological taxonomy in psychiatry.[49] From now onwards, the focus of child psychiatrists and of psychiatry in general, predominantly shifted towards an ontological understanding of disease and a biomedical model of mental disorder with 'intellectual inspiration derived from Kraepelin, not Freud' (Bayer and Spitzer (1985) quoted in Young, 1997: 99).

Constraining elements of ontologically distinct disease entities

Fleck pointed out some of the characteristic difficulties that arise and only make sense within this particular style of medical thought,

> As soon as medical thinking has found a certain ideal type in an infinite plurality of apparently atypical morbid phenomena, it faces a novel problem: how to reduce them to a common denominator, to obtain, by way of analysis, certain common elements, some component bricks from which the observed phenomena could be reproduced. In this way elements of morbid anatomy and morbid physiology arise. However, combinations of the motifs obtained in this way … never do adequate justice to the entire wealth of the individual features of the disease. (Fleck, 1927/1986: 41)

[49] See Young (1997, Chapter 3) and Mayes and Horwitz (2005) for more context on the *DSM-III* and the revolution in the classification of mental illness.

This outline of the logical consequences of medical thinking in terms of disease entities matched later developments in autism research prophetically. As I already mentioned, the search for a 'common denominator' started soon after Kanner described the plurality of morbid phenomena he associated with autism. Out of a number of initial characteristics, such as limited spontaneous and varied activity and monotonous and repetitive verbal utterances and behavior (Kanner, 1943), Eisenberg and Kanner (1956) later chose two necessary and sufficient features: 'extreme self-isolation and the obsessive insistence on the preservation of sameness, features that may be regarded as primary' (1956: 557). Soon after, these two features were considered too general and were no longer believed to capture the entire complexity of autism. Influenced by new types of investigation and new experimental and epidemiological methods, autism researchers decided that 'the central problem, present in even the most mildly handicapped autistic people, appears to be a specific difficulty in handling symbols, which affects language, nonverbal communication, and many other aspects of cognitive and social activity' (Ricks and Wing, 1975: 214). For some time, it was not social withdrawal but language deficits that were essential and necessary for an autism diagnosis (Rutter, 1968). This shifted again in the 1980s and at present, it is no longer language problems but deficits in social cognition and social interaction that have become essential in autism (Verhoeff, 2013/Chapter 3; Wing et al., 2011). In this process of redefining autism in terms of its essential features and primary deficits – that, as we will see, also takes place at biological levels – autism appears in modified forms, with new properties, and with new relations to and distinctions from other mental disorders.

Furthermore, besides the desire to reduce complex clinical pictures to primary and essential elements, 'the omnipresence of conflict and negotiation at the boundaries of particular ills' (Rosenberg, 2003: 500) is inherently related to the contemporary style of medical thought. In fact, part of the search for a common denominator is the ongoing intraprofessional controversy surrounding the proper categorization and demarcation of autism. Initially, controversy arose over whether autism was a subcategory of schizophrenia. Leo Kanner considered that early infantile autism 'may be looked upon as the earliest possible manifestation of childhood schizophrenia' (Kanner, 1949: 419). Later expert discussions, for instance, concerned if and how autism differs from other language disorders (Rutter, 1978), whether autism and Asperger's

disorder are essentially similar (Schopler, 1996), whether and how autism and Asperger's disorder differ from schizoid and schizotypical personality disorders (Tantam, 1988), how repetitive behavior in autism is different from repetitive behavior in mental retardation (Bodfish et al., 2000), if autism and psychopathy share an underlying cognitive profile (Rogers et al., 2006), how lack of empathy is different in autism compared to lack of empathy in psychopathy (Jones et al., 2010), how autism and ADHD are both similar and different (Gargaro et al., 2011), whether social communication disorder is part of the autism spectrum (Ozonoff, 2012), and so on. Without the contemporary style of thinking in terms of ontologically distinct diseases, these constant comparisons between disorders and the difficulties inherent in demarcating categories would be unthinkable or meaningless.

The continuous dynamic of searching for common ground, negotiating the essence and borders of autism, relating autism to other conditions, being unable to do adequate justice to the complexity of the clinical picture, and shifting emphasis to other 'component bricks' at phenotypical – but also cognitive and biological – levels, has been and still is an important driving force of autism research. It can even be argued that the conceptual changes, new categories, the construction of hypotheses, guessing about non-observed relations and the continuous search for autism's essence are necessary for the persistence of autism as a legitimate object of scientific scrutiny. With the idea of autism as an ontologically distinct disease, paradoxically, stability and endurance requires conceptual adjustments and consequently, a shifting image of autism.

Social entities and the bureaucratic imperative

Conflicts and negotiation at the boundaries of particular disorders are not restricted to intraprofessional controversies. Distinct categories inevitably involve including some people as well as excluding others. Wide-ranging issues such as insurance reimbursements, accountability for crime, responsibility for unwanted behavior or pain and suffering, but also issues concerning medical evidence, objectivity and authority are at stake in delineating diseases. They are a logical consequence of the (social) reality of distinct diseases. Each with their own ideas, backgrounds and interests, medical doctors, patient advocacy groups, governments, insurance companies, pharmaceutical companies, etcetera, play their part in establishing and shaping the boundaries of particular diseases.

Although Fleck mainly focused on the role of perception and cognition in his history of the Wasserman reaction, he also mentioned the role of consensus conferences and legislation in the 'genesis and development of a scientific fact' (Löwy, 2004b). The 'thought collective' of serologists, he clarified, 'standardized the technical process with genuinely social methods, at least by and large, through conferences, the press, ordinances, and legislative measures' (Fleck, 1979: 78, quoted in Löwy, 2004b: 519). Rosenberg (2003) further emphasized the practical importance of disease categories in their relationship to the management and administration of health care. 'Disease', he argued, 'does not exist in the domains of the clinical and bureaucratic practice as a general quality or experience: without a specific diagnosis it remains largely invisible – unreadable – to the world of clinical medicine' (2003: 499). Rationalizing tendencies within medicine, such as diagnostic procedures (for example, DSM categories), standardized treatments, clinical trajectories, and the governing rules of evidence-based medicine and randomized clinical trials, in combination with the needs of bureaucratic systems (for instance, regarding the Individuals with Disabilities Education Act (IDEA) or reimbursement procedures) create an additional constraint toward the construction and preservation of discrete disease categories. 'Disease categories serve', Rosenberg explains, 'as integrating mechanisms, facilitating countless microdecisions and thus linking different parts of the health-care system in a way that seems both necessary and proper' (ibid.).

Other important actors are disease and disability (self-) advocacy groups that are typically organized around specific disease categories. Autism has been a very significant locus of organization and activism. Starting in the 1960s in the UK and the US, parents have organized to share experiences and information, and to lobby for better services for their children (Silverman, 2011). In addition, partially as a reaction to dissatisfaction with psychoanalytical approaches and Bruno Bettelheim's by that time popular theory that autism was caused by cold, emotionally distant mothers (Bettelheim, 1967), parent advocacy groups lobbied for and contributed to a reconceptualization of autism as a biological disorder. Organizations like the US-based *Autism Speaks*, which is the biggest and probably most influential autism advocacy group, have a substantial impact on research directions through their research funding programs. From different perspectives and with different convictions and priorities, exoteric communities of parents of children with autism have, for instance, worked together to shape

research on the genetics of autism (Silverman, 2007) and to investigate the possibility that autism is caused by vaccines (Hobson-West, 2007).

Furthermore, other exoteric autism organizations and societies have played a significant role in raising public awareness about autism using, amongst many other means, worldwide fundraising and awareness-raising events.[50] These advocacy groups have been crucial in the identification of autism as an object of urgent global mental health concern. Meanwhile, other social movements, such as the neurodiversity movement, believe that autism is not a disease to be treated but rather 'a human specificity (like sex or race) that must be equally respected' (Ortega, 2009: 426). Although these various exoteric groups have different priorities, their activities are bounded by and organized around the central category of autism. Through autism awareness campaigns, activism on services and research funding, and the identity politics of the autism self-advocacy movement, autism groups not only reshape but also stabilize and popularize the very idea of autism.

The DSM-trained clinical gaze of mental health professionals, together with the bureaucratic needs of health administration, the clinical and scientific utility of disease categories and the organization of autism-oriented advocacy groups, all imply a bias toward seeing and thinking about autism as an ontologically distinct psychiatric and scientific entity. Furthermore, the borders of different autism communities are highly porous and open to multidirectional pressures and exchanges of ideas and individuals. Susan Swedo, for instance, is not only the chair of the *DSM-5* Neurodevelopmental Disorders Work Group and a researcher in the field of neuropsychiatry, but also a member of the scientific advisory board and a reviewer of grants for *Autism Speaks*. Similarly, founder of the UK-based *National Autistic Society*, Lorna Wing, is also one of the most influential autism researchers and the mother of an autistic child, and Bernard Rimland, research psychologist and father of an autistic child, founded the *Autism Society of America* and was a widely acknowledged autism authority. Fundamental research, clinical practice, autism advocacy and personal involvement have always been closely linked in the history of autism, with autism as a central and connecting object that intellectually unifies the multiple levels and various aims and practices of this broad and heterogeneous thought collective.

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[50] See: http://www.autismspeaks.org/what-autism/world-autism-awareness-day, accessed February 4, 2014.

Neurobiological specificity: the neuromolecular style of thought

Beginning at the end of the nineteenth century, germ theories – in combination with the rise of pathological anatomy, chemical pathology, and studies of normal and abnormal physiological functioning – constituted a strong case for a reductionist and mechanism-oriented way of thinking about the body and poor health. Similar to the ontological understanding of disease, this way of thinking has not been as steady in psychiatry as in the rest of medicine. Only in the last twenty to thirty years have psychiatric ailments been primarily thought of as biological disorders, with the brain being the central organ in which disease-specific somatic mechanisms are localized.[51] In the context of recent developments in the neurosciences, life sciences and biomedicine – for instance, in molecular genomics and neuroimaging – mental disorders are more and more located at the neurobiological level of the brain.[52] Contemporary psychiatry is part of a thought collective that consists of a broad range of neuroscientific disciplines, from neurogenomics to neuroaesthetics and social

[51] Developments in the production and use of psychotherapeutic drugs played a significant role in the emergence of a brain-centered, neuromolecular seeing and understanding of human beings and their cognitive, emotional, and volitional states. The introduction of novel psychotherapeutic drugs in the 1950s and 1960s played an important role in a new way of linking the brain and psychiatric disorders – through a 'neuromolecular gaze'. As Rose and Abi-Rached (2013) explain, throughout the 1950s, a number of decisive studies discussed the effects of novel psychotropic drugs, notably chlorpromazine, reserpine and imipramine, on mood and on psychotic and behavioral disturbances. Gradually the idea emerged that these drugs produced their clinically useful effects by acting upon the level of neurotransmission by influencing the amounts of monoamines (a group of neurotransmitters including serotonin, norepinephrine and dopamine) in the brain. A consensus began to arise that specific disorders were caused by anomalies in specific classes of neurotransmitters (Healy and McMonagle, 1997; Moncrieff, 2008).

[52] The brain as locus of mental pathology and target for treatment is certainly not a recent phenomenon. In mid-twentieth century asylums, brain-directed treatments were widespread. These treatments included electroshock therapy, insulin-induced coma and, to a lesser extent, brain surgery (see Sargant and Slater, 1948). However, if, where and how these unspecific and harsh therapies worked remained mysterious. Furthermore, mid-twentieth century corporeal understandings of emotion, behavior and cognition were very different from the recent pervasive and 'techno-somatic' understandings of specific mental disorders as being grounded in specific anomalies in the depths of the brain (Pickersgill, 2009).

neuroscience, unified by a particular style of thought.[53] Rose and Abi-Rached (2013) enumerate some of the key structuring principles of this 'neuromolecular style of thought':

> All mental processes reside *in the brain* (where else could they reside!), and each mental process will reflect, or be mediated by, or have something variously described as a correlate, an underpinning, or a basis, in brain events. Thus any mental state or process (normal or abnormal), will have a relation – exactly what relation is in dispute – with a potentially observable material process in the organic functioning of the neuromolecular processes in the brain. (Rose and Abi-Rached, 2013: 43)

Furthermore, within the neuromolecular style of thought, neural brain processes can and should be anatomized at a molecular level and investigations should proceed in a reductionist mode by exploring the fundamental elements of brain functioning. A key element of brain functioning is communication along and between neurons, that is neurotransmission. Besides different types of neurons and neurotransmitters, neurotransmission also involves 'the function of multiple other entities: ion channels, transporters, receptors, enzymes that catalyze or metabolize neurotransmitters at different rates, and so forth'. These entities are involved in all sorts of processes of neuronal motility, axon guidance, synaptogenesis and other aspects of neurodevelopment, and 'variations in each of these elements have functional significance and can in principle account for processes at higher levels' (ibid.).

Two major influences on this new way of thinking about mental disorders were the 'dopamine hypothesis of schizophrenia' (Carlsson and Lindqvist, 1963), which suggested there was a link between high levels of dopamine in the

[53] There are many kinds of explanations for the rise of a 'biological psychiatry' and the current dominance of the neurosciences in psychiatry. Often mentioned explanations are; the promising introduction of chlorpromazine as the first antipsychotic drug; dissatisfaction with unsuccessful psychoanalytic treatments of schizophrenia and the decline of psychoanalytic prestige in general; the infamous power of drug companies with their focus on neurobiological anomalies and their close ties with academic psychiatry; biopolitical forces oriented towards the medicalization of social problems; the seductive allure of 'objective' neuroscientific explanations and brain pictures; the activism of parents and support groups and the hopes and promises for a 'genuine' cure; and more (see, for example, Rose, 2007).

brain and schizophrenia, and the 'catecholamine hypothesis of depression' (Schildkraut, 1965), which suggested a link between depression and a deficiency of norepinephrine at particular adrenergic receptor sites in the brain. According to Rose and Abi-Rached (2013: 37), these studies marked an important moment 'when a new language was assembled together, one that would come to shape the [neuromolecular] style of thinking' that connected neuroscience with clinical psychiatry through pharmacology.[54] The research path of neuropsychiatry headed for a future in which psychiatric classification and diagnoses could be based on the specific neurochemical malfunctions of neurotransmitter systems. This 'neuromolecular gaze' not only provided psychiatry with new types of explanations, but shaped what counted as a valid explanation and constrained the kind of problems that needed to be solved.

Blurred boundaries and neurobiological underpinnings

Rose and Abi-Rached (2013) furthermore argue that the neuromolecular image of the brain blurred two historically important boundaries in psychiatry. They first mention the 'Cartesian boundary', which had been crucial since the birth of psychiatry as a distinct medical discipline in the mid-nineteenth century (see Davidson, 1999), between organic and functional disorders. The strict distinction between disturbances of mental functioning caused by identifiable lesions in the brain (organic) or caused by stressful events, life history or suppressed desires (functional) blurred when all mental disorders or disturbances of mental functioning must, at a fundamental level, be related to neuromolecular anomalies in the brain. Something similar applies to the distinction between 'states' and 'traits', a distinction that often characterizes the division between psychiatry and psychology. If both states (that is, intermittent periods of illness) and traits (that is, pervasive features of personality of character) 'essentially were variations of the same molecular mechanisms, that

[54] Even though the catecholamine hypothesis of depression and the dopamine hypothesis of schizophrenia 'proved to be wrong, perhaps fundamentally so', these 'two founding myths of the psychopharmacological imaginary' (Rose and Abi-Rached, 2013: 37) and the style of thinking they accompanied, would come to dominate the field of psychiatry. For a couple of decades, 'the biogenic amine system in the brain would increasingly become the obligatory passage point of all accounts of mental disorder' (ibid.). Whether there were environmental, genetic, psychodynamic, social or biographical factors in the etiology of mental disorder, they would have their effects through this biogenic amine system.

distinction blurred, and along with it the distinction between personality disorders and psychiatric illnesses – perhaps, even, the disciplinary divide between psychology and psychiatry when it comes to intervention' (Rose and Abi-Rached, 2013: 46).

Interestingly, the recently published *DSM-5* (APA, 2013) removed the common multi-axial classification system consisting of personality disorders and intellectual disabilities on a distinct axis from other mental disorders (such as anxiety disorders and schizophrenia), in favor of a nonaxial system. Even though, particularly for practicing mental health professionals, the neuromolecular style of thought should not be thought of as universally accepted and distributed, in general, mental disorders are no longer conceptualized in Freudian psychodynamic terms or as psychological reactions to personal and social adversities. In essence, mental disorders have become disorders of the neuromolecular structures of the brain.

Part of this neurobiological image of mental disorders consists of the neuropsychiatric efforts and hopes to demarcate mental disorders in neurobiological terms using genetic biomarkers and patterns of brain activation. The initial goal, which eventually was found to be premature, for the new *DSM-5* classification system of mental disorders was to 'translate basic and clinical neuroscience research relating brain structure, brain function, and behavior into a classification of psychiatric disorders based on etiology and pathophysiology' (Kupfer et al., 2002: 70). Steven Hyman, the former director of the NIMH, acknowledged in 2007 that 'it is probably premature to bring neurobiology into the formal classification of mental disorder', however, he argued, 'it is not too early to use neurobiology as a central tool to rethink the current approach to mental disorder' and he expressed a hope that future manuals 'can usefully incorporate information about brain structure and function' (Hyman, 2007: 725). In similarly promising terms, current NIMH director Thomas Insel argued that 'reclassifying disorders based on brain function could yield a system of diagnosis based on biomarkers – biological signs such as brain activity patterns or chemical or structural changes specific to the condition' (Insel, 2010: 50-51). He rather boldly predicted that 'today's developing science-based understanding of mental illness very likely will revolutionize prevention and treatment and bring real and lasting relief to millions of people worldwide' (ibid.: 51).

For autism in particular, the expectations that neuroscience will solve diagnostic and therapeutic problems – that is, distinguish autism subtypes; demarcate pathology from normality; gain understandings of etiology; screen presymptomatic individuals; and develop effective treatments that aim at specific neurobiological underpinnings – have been and still are high. Since approximately the 1970s, with the decline of psychoanalytic prestige, the revival of Kraepelinian thinking, and in the spirit of the emerging neuromolecular style of thought, autism has become a yet-to-be-identified biological thing. However, much like every other mental disorder, autism has turned out to be extremely hard to pin down on a specific neurobiological basis.

Autism and neuroscience

Despite the overarching neuroscientific tendency in psychiatry, autism research has its own particular link with neuroscience. Autism parents have played an important role in pushing autism research in a predominantly biological direction (Eyal and Hart, 2010; Silverman, 2011). This involvement is often interpreted as a reaction to Bettelheim's influential psychoanalytically founded theory that autism was caused by 'the parent's wish that his child should not exist' (1967: 125). However, it was a few years before Bettelheim's book that the previously mentioned autism parent and researcher Bernard Rimland proposed the first consistent neurological theory of autism when he suggested that autism was caused by malfunctions in specific parts of the brainstem (Rimland, 1964). From that period onward, biological and neurocognitive research on autism expanded exponentially.

Another important source of support for the biological approach to autism, against psychoanalytical theories, was the first and very influential autism twin study (Folstein and Rutter, 1977). This study brought 'the importance of genetic factors in the aetiology of autism … [and its] very high heritability' (p. 307) to the attention of autism research and later heritability studies confirmed extremely high heritability rates of between 85 and 92 per cent (see Miles, 2011). This study marked the beginning of an extensive search for autism genes carried out by disciplines ranging from epidemiology to molecular genomics and with a variety of statistical methods ranging from twin and linkage studies, to association studies with candidate genes and whole-genome association studies (see, for example, Abrahams and Geschwind, 2008). This ambitious and complex search yielded no easy route from gene(s) to disorder. The number of

genes associated with autism may be a couple hundred or more; they are probably not specific for autism and the most common mutations are found in less than one per cent of the children with autism (Schaaf and Zoghbi, 2011). Sanders et al. (2011) even stated that between 130 and 234 submicroscopic chromosomal deletions and duplications (copy number variants or CNVs), which vary widely in function, are linked to autism. These rather ambiguous results further complicated the search for autism's underlying neurobiology.[55]

In the meantime, at different neurobiological and cognitive levels – situated in the black box between genes and the phenotype – various lines of neuroscientific research have attempted to provide specific and unifying accounts of autism. The 1980s and 1990s saw the rise of a couple of key cognitive theories of autism (Hollin, 2013; Verhoeff 2013/Chapter 3). For example, a defective 'theory of mind', which is the inability to attribute mental states to other individuals (see Baron-Cohen et al., 1985); 'weak central coherence', which refers to a lack of conceiving a meaningful whole picture in combination with an overemphasis on detail (Frith and Happé, 1994); and impaired 'executive functioning', which refers to problems in planning and other problem-solving capacities (Ozonoff et al., 1991), have all been proposed as a cognitive 'common denominator' and, therefore, as being fundamental to autism. However, despite their influence on thinking about autism, it is now widely accepted that none of these cognitive theories can explain all the behavioral phenomena associated with autism (Happé and Ronald, 2008).

Other searches for neurobiological singularity have focused on structural anomalies in the entire brain and in specific brain areas. For instance, abnormal enlargement of total brain volume (Sparks et al., 2002), increased white matter compared to gray matter (Herbert et al., 2004), enlargement of the frontal lobes (Carper et al., 2002), enlargement of the amygdala (Schumann et al., 2004) and enlargement of the cerebellum (Hardan et al., 2001), have all been associated with autism. Yet again, none of these studies has been able to get a grip on the specific neurobiology of autism (Amaral et al., 2008). Furthermore, individuals with autism may or may not have neurotransmitter abnormalities in dopamine, serotonin, or glutamate systems, or abnormalities in the neurohormones oxytocin and vasopressin (Insel, 2010). The most recent focus in autism

[55] See Jeste and Geschwind (2014) for a recent review on genetic findings in ASD research and their expectation to identify specific autism subgroups based on 'genetic classifiers'.

neuroscience is on functional, instead of structural, problems of the brain. With functional neuroimaging and molecular genetics studies, abnormalities in neural networks (Peca and Feng, 2012), mechanisms of synaptogenesis (Persico and Bourgeron, 2006), and problems in the connection between different brain areas are the new hopes for a coherent neurobiological account of autism. Yet, despite current efforts, the neurobiological basis of autism remains unidentified (Rutter, 2011; Waterhouse, 2013).

Where does that leave us for a neurobiology of autism? To quote Rose and Abi-Rached (2013: 138) again: 'each of the pathways that neuropsychiatry has attempted to trace through the brain seems to run, not into the bright uplands of clarity, but into the murky, damp, misty, and mysterious forests of uncertainty'. As with other mental disorders, the 'hard residue of material reality' resists a straightforward translation of autism into biological terms. Currently, despite the neuroscientific dominance of autism research, no clear autism biomarkers have been found that support diagnostic practices, distinguish autism subtypes, guide the development of new treatments, or demarcate pathological from normal conditions. Autism diagnosis and classification remain behaviorally based. Yet, still guided by an ontological (Temkin, 1977) understanding of autism and not less constrained by the neuromolecular style of thought, neuroscientific research on autism has readapted its attempts to identify neurobiological singularity towards developmental processes, epigenetics and neuroplasticity. The ambiguous findings of many genes, multiple brain areas, different cognitive profiles and heterogeneous diagnostic features need to be connected in a novel way. In the neuromolecular style of thought and with the need to take neurobiological heterogeneity and dimensions of time, plasticity and interactions with the environment into account, autism has become a neurodevelopmental spectrum disorder.

Rise of a neurodevelopmental spectrum disorder

Besides neurobiological heterogeneity, there is another profound uncertainty that surrounds autism research: the heterogeneity of the phenotype itself – the clinical picture with all the signs and symptoms associated with autism. This problem of heterogeneity relates to the increasing struggle to hold autism

together as a convincingly steady diagnostic category (see also Fitzgerald, 2012; Hollin, 2013).

A crisis of heterogeneity

Many autism experts have come to argue that 'the central challenge to understanding autism has been its heterogeneity' (Waterhouse, 2013: 3). Diagnostic features including social interaction impairment, repetitive and restrictive behaviors, and sensory abnormalities as well as non-diagnostic features such as savant skills, intelligence, language skills, perceptual problems, motor disorders, neurological disorders (epilepsy), ADHD symptoms and environmental risk factors vary widely in form and severity among those diagnosed with autism. 'If you've seen one child with autism, you've seen one child with autism. Autism's like a snowflake', is the often heard quote from autism researcher Robert Schultz (Scott, 2011). Autism researcher Lynn Waterhouse (2013) devoted an entire monograph to this issue of heterogeneity.

She states that variation in patterns of impaired sociability has been found for all developmental stages. For instance, some infants later diagnosed with autism 'paid no attention to social stimuli as babies, smiled infrequently, and vocalized little. However, this was not true for all, because many infants later diagnosed with autism did smile, vocalize, and pay attention to other people as infants' (Waterhouse, 2013: 7). Some toddlers with autism do not respond to their name, never reach to be picked up, or have limited eye contact and social interaction with parents. Yet, other toddlers with autism do not lack this type of interactive behavior. The same is true for autistic children who may or may not initiate social interaction, show empathy, or use appropriate gestures along with speech. Likewise, other diagnostic features such as rigid interests and repetitive behaviors have also been found to be heterogeneous. Preoccupation with restricted interests; non-functional routines or rituals (an inflexible need for the same route or the same clothing); and repetitive motor mannerisms (for example, flapping hands or spinning in circles) are all found in various forms, combinations and levels of severity (ibid.).

Guided and constrained by an ontological understanding of autism and the idea of neurobiological specificity, attempts to understand and deal with variation have alternated between searching for biologically and behaviorally homogeneous subgroups (see, for example, Jeste and Geschwind, 2014; Lui et al., 2008; Ingram et al., 2008), and reducing the complex clinical picture of

autism to a common (underlying) denominator (see Verhoeff 2012/Chapter 2). However, as I have shown above, researchers have not been able to identify either a unique, unifying brain (or cognitive) deficit or meaningful subgroups. 'There is now', Waterhouse (2013: 23) argues, 'a large pile of competing orphaned, and unsynthesized theories of autism subgroups, and theories of unifying brain deficits and unifying patterns of genetic and environmental risk factors for autism'.

The vast clinical heterogeneity in the manifestation of autism, including course, prognosis, response to treatment and co-morbid conditions, in combination with the difficulties of identifying specific neurobiological markers or cognitive profiles, created serious scientific challenges. It destabilized the understanding of autism as a separate neurobiological disease and produced a need for a reworking of the very idea of autism. Yet, bound by the stylized readiness for perceiving and thinking about autism and related conditions as ontologically distinct diseases, and by autism's bureaucratic function in integrating different parts of the health-care system, reframing autism is a delicate process. It is a process of stabilization and harmonization that takes place at the nexus of 'exoteric' and 'esoteric' circles inhabited by neurobiological researchers, psychiatrists, medical practitioners, health administrators and patients and their advocates. The emergence of the 'autism spectrum' as the new central object of study can be seen as an important moment in this process, in which the ontological understanding of disease and neuromolecular styles of thought persist, whereas this new image of autism can account for many of the difficulties and ambiguities produced by recent autism research.

The spectrum idea of autism

As I stated earlier, the meaning of the term 'spectrum' in relation to autism is ambiguous, and the shift towards scientific endorsement, popularization and institutional acceptance of the autism spectrum is more gradual than radical. Autism researcher Michael Rutter had already mentioned in 1968 that in autism 'there seems to be a continuum from severe persistent social withdrawal to mild transient withdrawal' (Rutter, 1968: 20). Wing and Gould (1979: 26) also noticed a 'continuum of severity' in the social, language and behavioral impairments associated with autism and Lorna Wing introduced and popularized the idea of a triad of social impairment and the differences in

symptom severity, associated levels of impairment and clinical manifestation of these three cardinal features of autism as 'the autistic spectrum' (Wing, 1996). More recently, autism researchers have also used the spectrum concept to refer to the continuity of autistic traits between the clinical and the general population, and to refer to the variety of associated features (instead of the cardinal features described in DSM criteria) such as epilepsy and savant skills (see, for example, Williams et al., 2008).

Furthermore, the idea of the autism spectrum is currently used to reflect the variable manifestations across life span within and between individuals with autism (Happé, 2011). Lastly, it is important to note that Lai et al. (2013) mention another meaning of the autism spectrum, suggesting that the idea of a spectrum not only refers to phenotypical variation, but also has come to reflect the earlier mentioned neurobiological, genetic, cognitive and etiological (including potential environmental contributors) variation in autism. A spectrum of genes, neural networks, molecular mechanisms, neurocognitive and neurodevelopmental profiles, and etiological elements (Geschwind, 2011; Happé, 2011) has become part of the idea of an autism spectrum.

In the last couple of decades, the spectrum metaphor has repeatedly been used to indicate different levels of heterogeneity related to autism. In a cumulative manner, the use of the term expanded from different levels of symptom severity to diversity in symptoms, manifestations, impairment, course, prognosis, response to treatment and cognitive and neurobiological markers. Hacking (2009: 47) argues that the spectrum metaphor is problematic, as it 'suggests that you can arrange autistic people on a line, from more to less'. Without discussing the possible function of the spectrum metaphor or what it is that keeps the autism category together, Hacking prefers to speak of an 'autistic manifold' which is, I suggest, more or less what the 'spectrum' in autism research and practice has come to signify: heterogeneity at multiple levels. Nevertheless, the assumption that the autism spectrum or potential subgroups within the spectrum (for example, Asperger's disorder) have distinct brain-based pathophysiologies which explain, produce and underlie the symptoms, impairments and suffering experienced by autistic patients – that is, the ontological understanding of autism within the contemporary style of medical thought – remains unchallenged.

The recent 'official' shift to 'autism spectrum disorder' (APA, 2013) might not seem very different from earlier dimensional perspectives of, for instance,

Rutter (1968) and Wing (1996). However, despite the clear continuities in recognizing heterogeneity, I argue that it does indicate an important change in thinking about autism. With the latest advent of promising functional neuroimaging studies, molecular genetics studies and genome-wide association studies (GWAS), the persistent failures to identify autism's neurobiological pathophysiologies has become particularly challenging for the validity of autism as a neurobiological disorder. That is to say, within an ontological understanding of disease, the homogeneity of these underlying genetic and neurobiological elements is basically what indicates the validity and legitimacy of a separate disease category. In light of these disappointments, reframing autism as a spectrum disorder converts problematic and ubiquitous heterogeneity – including the 'existentially' challenging neurobiological and cognitive heterogeneity – into an intrinsic feature of the disorder. This reframing ensures the existence of an autism category; it postpones the problem of validity; and creates new opportunities for further neuroscientific research directed at fundamental and specific brain-based disease mechanisms.

As a comparison, the diversity in severity, symptoms and course in Down syndrome or Huntington's disease is widely acknowledged, but these well-defined (valid) genetic disorders are not considered spectrum disorders. The shift towards an autism spectrum disorder is not just about describing and acknowledging variation in severity and symptoms, but involves a reworking of the very object of explanation. With the reframing of autism as a somewhat vague and multi-interpretable spectrum disorder, diverse hypotheses concerning the now inherent neurobiological variation, for instance, aimed at complex networks of genes (Szatmari, 2011; Jeste and Geschwind, 2014) or converging molecular pathways (Sakai et al., 2011), have come into being. These are not just new explanations of autism; the object of investigation has been modified, facilitating further research and a range of new types of hypotheses and explanations regarding the validity – that is, neurobiological specificity – of the new autism spectrum.

In a discussion on the *DSM-5* category of ASD, Rutter (2011: 399), for instance, concluded that 'at the moment … it is highly likely that there are meaningful subcategories of autism spectrum disorders but that these are not well identified'. Holt and Monaco (2011: 455) suggested that 'genetic research is validating the view that ASDs should not be considered a set of discrete disorders, but a continuous range of individually rare conditions', and Boucher

(2011) hypothesized that the autism spectrum reflects many brain deficits and varied etiologies that must in some way interact to converge on a single specific brain abnormality. As members of the *DSM-5* Task Force, Kupfer and Regier (2011: 673) stated that 'the proposal for a single "autism spectrum disorder" category … was born from data suggesting that these disorders [Asperger's disorder, autistic disorder, PDD-NOS] share a pathophysiological substrate'. Somewhat more specifically, Kana et al. (2011: 428) argued that 'given the complexity, heterogeneity, and the developmental nature of ASD, a global explanation or a set of explanations seems optimal. We believe that disrupted cortical connectivity may be one such explanatory model that provides a comprehensive outlook'.

Thus, while the powerful autism-oriented advocacy organizations, the need to regulate administrative and clinical practices, and the DSM-trained gaze of clinicians, autism experts and other mental health professionals are important forces that hold autism together as a diagnostic category, a reworking of the construct of autism towards a spectrum preserves the existence of autism as a scientific object in search of neurobiological specificity. Despite all the ambiguity and uncertainty that surrounds the neurobiology of autism and pressured by the need for successful translations between fundamental neuroscientific research and goal-oriented clinical applications, the move towards an autism spectrum protects autism's threatened scientific status as a valid neurobiological disorder – a status that equally legitimizes many of the more exoteric practices and communities in which autism circulates.

In sum, at a moment when biological and categorical approaches towards autism face serious empirical difficulties, a delicate balance is established that holds together and integrates the dominant neuromolecular style of thought and the current style of medical thought in terms of ontologically distinct diseases. The emergence of an autism spectrum satisfies the scientific, institutional and socio-political needs for continuity, homogenization and unification of neuroscientific research, clinical practice and the bureaucratic space of special services, reimbursements and health administration. Both within and between the 'exoteric' and 'esoteric' circles of the autism field, stability and commensurability is at stake in reframing autism. However, this need for stability and commensurability comes at a cost, as the particular objectives of specific research groups, clinicians, and advocacy groups might not be best achieved through a unifying autism spectrum disorder.

Concluding remarks

As current director of the NIMH Thomas Insel argues:

> With no validated biomarkers and too little in the way of novel medical treatments since 1980, families need science to provide more than hope. Genetics and neuroscience finally have the tools to transform the diagnosis and treatment of mental illness. But first, it is time to rethink mental disorders, recognizing that these are disorders of brain circuits likely caused by developmental processes shaped by a complex interplay of genetics and experience. (Insel and Wang, 2010: 1971)

Yet, as Insel and Wang try to open up space to rethink mental disorders, 'the free unfolding of ideas' (Fleck, 1979: 84), or the amount of freedom to rethink mental disorders is rather limited as mental disorders have already become 'disorders of brain circuits'. Contemporary academic psychiatry remains committed to the neuromolecular style of thought and following autism, psychotic disorders, bipolar disorder, obsessive-compulsive disorder, and other, are gradually modified and appear in neurodevelopmental and spectrum terms that still hold disease categories together. The case of autism shows that despite the failure to identify specific and clinically relevant biological markers, the current transformation in thinking about specific psychiatric disorders as a neurodevelopmental spectrum disorders enables the continuity of neuropsychiatric research and releases tension from the general disappointments and unfulfilled promises and hopes for a neuroscientific foundation of psychiatry in general.

Why is this a good moment to disentangle the prevailing styles of thought that directed the emergence of a neurodevelopmental autism spectrum? As Fleck pointed out, 'the more developed and detailed a branch of knowledge becomes, the smaller are the differences of opinion' (1979: 83). A dense network of active and passive connections that constitutes a particular style of thought seems to achieve a kind of inevitable stability and a 'tendency to reify and objectivize the conceptual creations of scientific thought arises' (ibid.: 144). However, now that we are still close to this process of reframing and stabilizing autism, the dominant socially and historically preconditioned ways of seeing and thinking about autism become less compelling and no longer seem

inevitable. In the current scientifically uncertain times, in which 'neuropsychiatry [has] not been able to "self-vindicate"' (Rose and Abi-Rached, 2013: 138), and in which the communities that are involved are increasingly diverse in their practices, aims and interests, the harmony of autism as a central structuring concept is not self-evident and the traces of labor invested in keeping this heterogeneous field together are not yet erased. A consideration of these traces of labor and the historically contingent processes through which the neurodevelopmental autism spectrum comes into being makes us realize where our contemporary psychiatric categories, our preconditioned ways of seeing and thinking, and our ways of organizing, treating and investigating psychiatric ailments come from.

The recent emergence of a neurodevelopmental autism spectrum illustrates the multitude of interactions within its heterogeneous 'thought collective,' and can be seen as an exemplary case of the outcome of a close intertwining of abstract understandings of disease, the clinical gaze of health professionals, techniques that enable the visualization of neurobiological phenomena, epidemiological studies, the practical needs of clinicians, specific advocacy groups and regulatory practices. A network of active and passive elements of knowledge, taking neurobiological research seriously and recognizing the socially and historically contingent determinants and constraints of particular styles of thought, effected the reframing of autism as a neurodevelopmental autism spectrum and the new way of seeing this particular phenomenon.

In this paradoxical process of stability through change, the modified concept of autism fosters new hypotheses and spaces of experimentation in the continuous search for autism's neurobiological foundation. However, whether this search will result in valuable translations of fundamental research into clinical practice is very uncertain. Given the diversity of the aims of clinicians, individual patients, neuroscientific researchers, epidemiologists, health administrators, advocacy groups, insurance companies, and other communities involved, it might be time to give up some of the coherence across these communities and to let go of the effort to keep this broad field together by a single autism spectrum. This should include a consideration of the benefits and disadvantages of an ontological understanding of mental illness and the related search for autism's neurobiological specificity.

Supposing, for argument's sake, that these conclusions regarding the rise of a neurodevelopmental autism spectrum disorder are sound, there remains the

question of how 'Fleckian' they are. One could argue that a true Fleckian account requires a more fine-grained sociological analysis of the different thought collectives, their members, how they interact, how they disagree and dispute and how, taking these dynamics into account, the spectrum approach has become the new way forward in the field of autism. It is certainly true that some collectives have not been sufficiently heard. The perspectives and influences of (and arguments against) conflicting positions, for instance of clinicians who oppose the ontological understanding of autism and of Asperger's disorder advocacy groups that make a plea against the autism spectrum and for a separate Asperger's disorder, have remained rather unanalyzed. Instead, with Fleck's conceptual tools I focused on those historically constrained ideas, practices and ways of perceiving that keep the autism field together and the research going. An analysis of how particular styles of thought directed the reworking of the idea of autism resulted in a story of stability and commensurability in which the multiplicity of ways in which autism is experienced and understood disappeared out of sight. For a more sociologically oriented approach of how these differences are negotiated within and between the thought collectives, indeed, a complementary study would be indispensable.

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